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# (54) SILK PROTEINS

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# Related U.S. Application Data

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- Provisional application No. 60/723,766, filed on Oct. 5, 2005.

#### **Publication Classification**

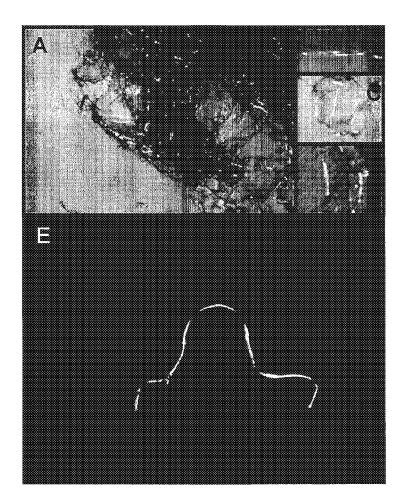
(51) Int. Cl. C07K 14/435 (2006.01)C12N 15/82 (2006.01)C12N 15/70 (2006.01)C12P 21/02 (2006.01)

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CPC ... C07K 14/43572 (2013.01); C07K 14/43563 (2013.01); C12P 21/02 (2013.01); C12N 15/8257 (2013.01); C12N 15/70 (2013.01); C07K 2319/00 (2013.01); C07K 2319/73 (2013.01)

#### (57)ABSTRACT

The present invention provides silk proteins, as well as nucleic acids encoding these proteins. The present invention also provides recombinant cells and/or organisms which synthesize silk proteins. Silk proteins of the invention can be used for a variety of purposes such as in the manufacture of personal care products, plastics, textiles, and biomedical products.



А

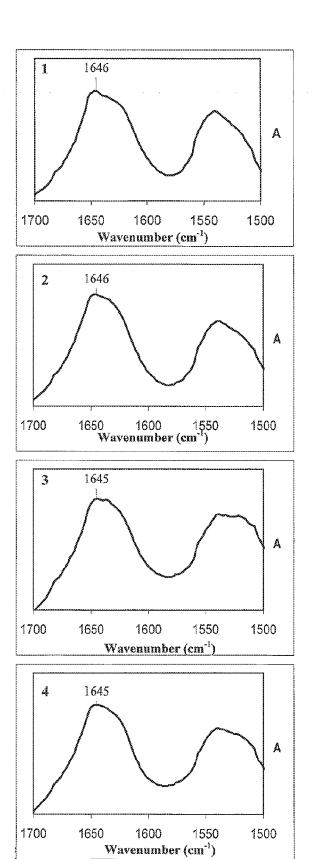


Figure 1

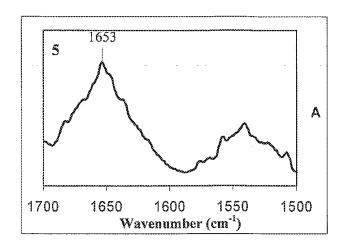


Figure 1 continued

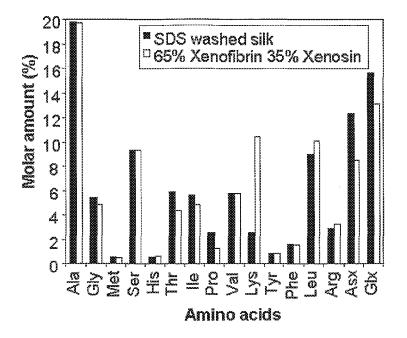


Figure 2

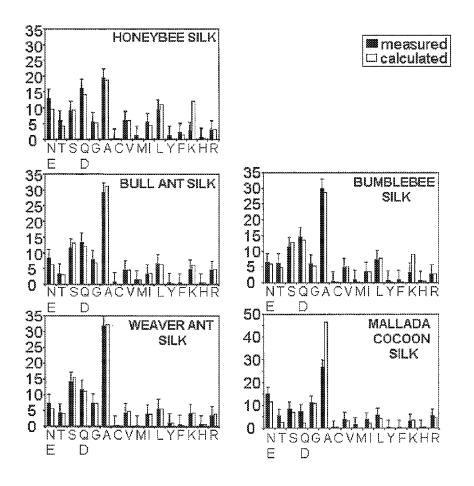


Figure 3

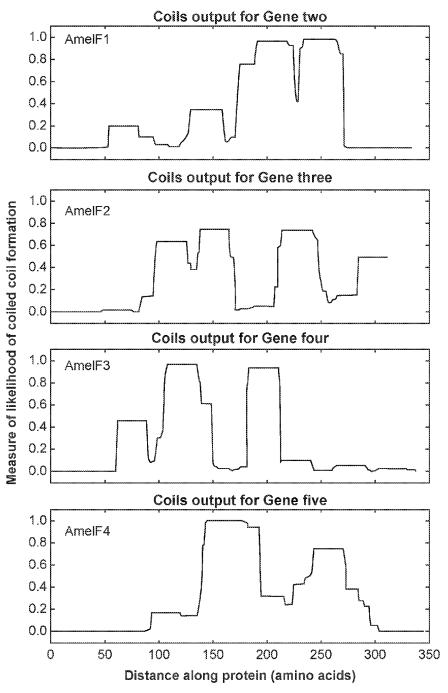


FIG. 4

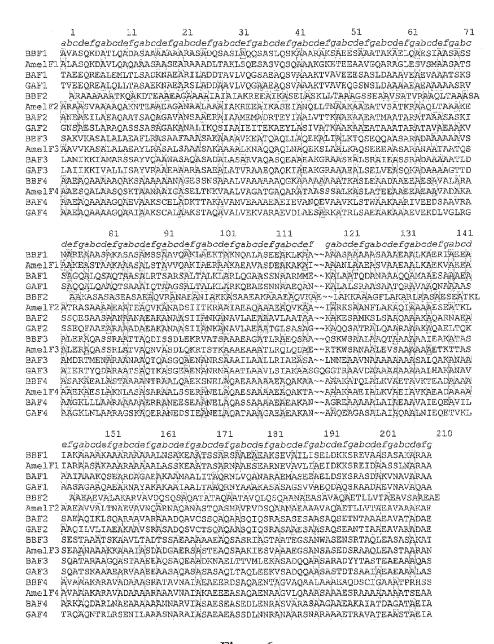
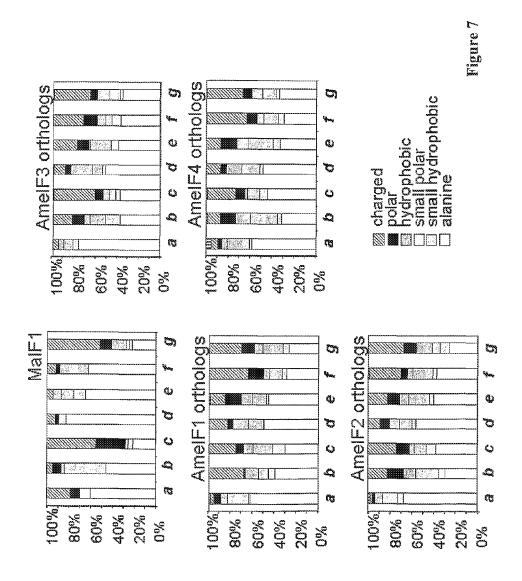


Figure 6



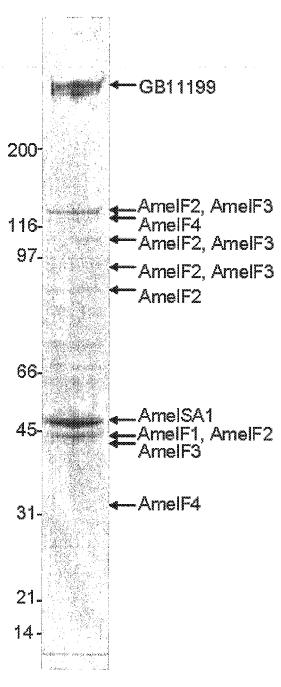
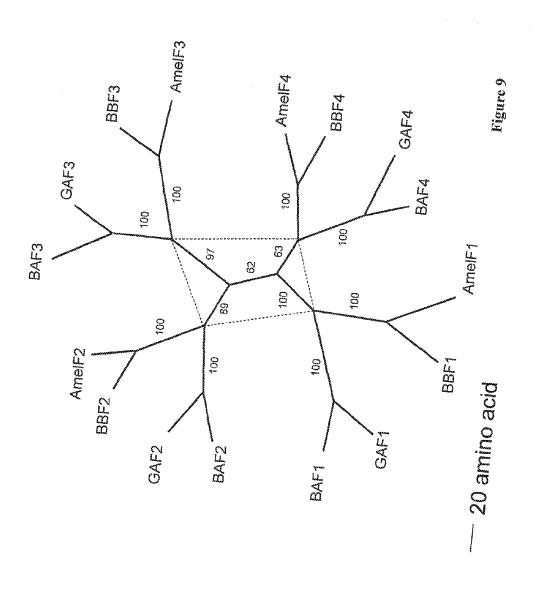


Figure 8





# A)

#### Xenospiral (SEQ ID NO:2)

MKIPVLLATCLYLCGFASAGLEGPGNSLPELVKGSÄSÄTÄSTÄVTÄRSGLRAGOVALASOKDAVLÇAQAA ASAASEARAAADLTAKLSQESASVQSQAAAKGKETEEAAVGQARÄGLESVSMÄÄSÄTSÄÄÄEASTAAKAA ASALSTAVVÇAKIAERAAKAEAVASDEAKAKAIAAANLAAEASVAAEAALKAEKVAEEAJARAASAKAAA RÄÄÄÄÄLÄSSKEAATASARNAAESEARNEVÄVÜJÄEIDKKSREIDÄÄSSLNARAAAKASSRNVETATIGÄ NINSSKQVVSIPVEIKKESEPEYSISWREDEEVTKEKKEHINLNDFDLKSNVF

#### Xenospira2 (SEQ ID NO:4)

MKIPAIFVTSLLVWGLAEGRVINHESLKTSEDIQGGYSAGIVGDGSDALGSSIENAQKVARĀAENVGLNI ELGAGARAASVAAAAQAKNTEAAEAGANAALAAAIAKREEAIKASEIANQLLTNAAKAAEATVSATKRAA QLTAAAKEATRASAAAAEAATEAQVKANADSIITKRAALABAQAAAEAQVKAATARKSAANFIAKAQIAA AAESEATKLAAEAVVALTNAEVAVMQARNAQANASTQASMAVRVDSQAANAEAAAVAQAETLLVTAEAVA AAEAEVANKAATFAKQIVNEKKIHVAKLE

#### Xenospira3 (SEQ ID NO:6)

MQIPTFVAICLLTSGLVHAGVEEFKSSATEEVISKNLEVDLLKNVDTSAKRRENGAPVLGKNTLQSLEKI KTSASVNAKAAAVVKASALALABAYLRASALSAAASAKAAAALKNAQQAQLNAQEKSLAALKAQSEEEAA SARANAATAATQBALBRAQASSRLATVAQNVASDLQKRTSTKAAABAAATLRQLQDABRTKWBANAALEV SAAAAAAETKTTASSBAANAAAKKAAALASDADGRERSASTEAQSAAKIESVAAAEGSANSASEDSRAAQ LEASTAARANVAAAVGDGAIIGLGEEAGAAACLLAQAKALAEVSSKSENIEDKKF

#### Xenospira4 (SEQ ID NO:8)

MKIPSILAVSLLIWGLASGAREEVETROKTKTSTVVKSEKVEVVAPAKDELKITSEPIFGRRVGTGASEV ASSSGEATAISLGAGQSAAESQALAASQSKTAANAAIGASELTRKVAALVAGATGAQARATAASSSALKA SLATEEAAEFAEAAVADAKAAAEKAESLAKKLASASARAALSSERAEELAQAESAAAAAAAAAAA AEIALKVAEIAVKAEADAAAAAVAAAKARAVADAAAARAAAVNATAKAEEEASAQAENAAGVLQAAASAA AESRAAAAAAAAATSEAAAEAGPLAGGMKPPHWKWERTPVKKEEWKTSTREFWKTTGREWEVK

#### Xenosin (SEQ ID NO:10)

MKYMLLLLSIFICAHIVCAGVNTELKKDGELKEESYEKSESKSLKEIKEERASKSKSERLKIREEKREEE EKSKSLDIJVVREKITKLSSWLKEEKDISPLJEERINGKGLLGLEDVTDELNIALKSLKEGKKFDTWKFEK GSEDVRSLEELDTSVELKLIKEGKTDRGATDLEKNGKVLVDLEKISENILETCGSQKKTVEVVDDKDK KWNKESGWKKNLNDLDWKKDLDKDKVGGGLLGGLSGLLNSLKSEKGLLGLLNKNQIELLIPLISEIKKKN TDFNLFBSVDSVERNLDLKLFTSSVSKVTELLNKGIDTQTILNARNGDEFDLSGKELKNVKGIFGLTGSLKRSLGLENIINLPFKRIPLLKF

#### B)

### BBF1 (SEQ ID NO:23)

#### BBF2 (SEQ ID NO:25)

MKIPAILVTSLLVWGGLAEGHVVKRDKELKAPALPELLGDGSDTLGASMENGIKVARASQNVGLRTELNA AARAAAAATKQAKDTEAAEAGAAAATAIAIAKREEAIKASELASKLLTAAAGSSEAAVSATVRAAQLTA AASAAAKASASASEASAEAQVRANAEANIAKKASAAEAKAAAEAQVKAELAKKAAAGFLAKARLAASAES EATKLAAEAEVALAKARVAVDQSQSAQATATAQAATAVQLQSQAANAEASAVAQAETLLVTAEAVSAAEA EAATKATSWGEECHQREKVTFSEDRLNERQDNW

Figure 10

#### BBF3 (SEQ ID NO:27)

MQIFAIFVTCLLTWGLVHAGSVELGAPKQESVLVEQLLLKNVETSAKRKENGAPKLGESTAAALASTKAT AAAEAKASAKVKASALALAEAFLRASAAFAAASAKAAAAVKEATQAQLLAQEKALIALKTQSEQQAASAR ADAAAAAAVSALERAQASSRAATTAQDISSDLEKRVATSAAAEAGATLRAEQSAAQSKWSAALAAQTAAA AAAIEAKATASSESTAAATSKAAVLTADTSSAEAAAAAEAQSASRIAGTAATEGSANWASENSRTAQLEA SASAKATAAAAVGDGAIIGLARDASAAAQAAAEVKALAEASASLGASEKDKK

#### BBF4 (SEQ ID NO:29)

MKIFSILAVSLLVWGLASAGKPLIANAQIGKVKTETSSSSEIETLVSGSQTLVAGSETLASESEALASKS EALTSEAETASVTTKDELILKGEAITGKKLGTGASEVAAASGEAIATTLGAGQAAAEAQAAAAAQAKSAA AAAANAGESSMSAAALVAAAAAAQGKAAAAAAAKKASLEAADAAEEAESAVALARAASAKAEALASTAA AANTRAALQAEKSNELAQAEAAAAAEAQAKAAAAAKATQLALKVAETAVKTEADAAAAAAVAAAKARAVAD AAASRATAVNAIAEAEERDSAQAENTAGVAQAALAAAEAQDSCIGAAATPRHSSSYAWWKLRITSLIVIL SPRNRRT

#### BBSA1 (partial) (SEQ ID NO:30)

GNSESGENWKNGESSESGKNWRNSGSSESGKNWKNGGSSESNKHWKNGGSSESGEKWKNSESSESGKNWK NSGSSESGKNWKNGGSSESGKNWKNGGSSESGKNWKNGGSSESGKNWKNGGSSESGKWKNSESGNKGKSSKSESWKSNINSKNDGSWKSSEE SEKWKDGKAVAEDSVSINWADVKEQISNIATSLEKGGNLEAVLKIKKGEKKISSLEIIKEKISVLLKWIQ EGKDTSSLLDLKEGSKDIASLKEIKGKILLIVKLVNEGKDTSGLLDLEASGKVILELQSAIEKVLVKSEK VTKVSEVSGLVKSKTVSDIKFLQAVIPLILELQKTDINLSTLNKWSTVNVNSIDKERVTKTVPVLLQSMK GGEDIQNLLSAKGAKKLGISALDLQAVQGALGVVGKLSSGGALNSKGLLNLKDGASVLGAGKIGGLIPLP KI.

#### BAF1 (SEQ ID NO:41)

MKIFAIIATSLLLWGFASASGPRLLGGRSAASASASASAEASAGGWRKSGASASAKAGSSNILSRVGA SRAAATLVASAAVEAKAGLRAGKATAEEQREALEMLTLSADKNAEARILADDTAVLVQGSAEAQSVAAAK TVAVEEESASLDAAAVEAEVAAATSKSSAGQALQSAQTAASALRTSARSALTALKLARLQGAASSNAARM MEKALAATQDANAAAQQAMAAESAAAEAAATAAAKQSEARDAGABAKAAMAALITAQRNLVQANARAEMA SEEAELDSKSRASDAKVNAVARAASKSSIRRDELIEIGAEFGKASGEVISTGTRSNGGQDAIATAEASSS ASAVGIKKTSGHWGSGKWSRVSKGKGWASSNADADASSSSIIIGGLKRGGLGSEASAAASAEAEASAGTL LI.

#### BAF2 (SEQ ID NO:43)

MKIPALLVTSLLAWGLASGRVIESSSSASAQASASAGSRGLLGKRPIGKLEWGKEEKKLEELDEESLNEA ALKVGIKNGGLDVAKGAAVLEAAMSDVATLTDQRSLVDLGLGPVANEAEILAEAQAATSAQAGAVANSAA ERAIAAMEMADRTEYIAALVTTKAAKAAEATMAATARATAAASASKISSQESAASAANAANAEAKANAAS IIANKANAVLAEAAAVLAATAAKAKESAMKSLSAAQAAAKAQARNAEASAEAQIKLSQARAAVARAAADQ AVCSSQAQAASQIÇSRASASESAASAQSETNTAAAEAVATADAEAAAQAEAWVMSLKNDLWLHLNMKGEA KAEGEAVSISKGHRGGIRSGSISEASAEASSNVSMGGRHGRKDLVSEALAGASAGSSADSI

### BAF3 (SEQ ID NO:45)

Figure 10 continued

#### BAF4 (SEQ ID NO:47)

MKIPATLATSILIWGLVGASELESEASAASAQAEASSSGRSGKLSASQASASASASASASAGSRGGSKGGW
GQLRRGDVKSEAKSAAAIAVEGAKIGTGIGNTASASAEALSRGLGIGQAAAEAQAAAAGQAEVAAKSCEL
ADKTTAKAVAMVEAAAEAELEVANQEVAAVKLSTWAAKAARIVEEDSAAVRAAAGKLLLAARAAAAAERR
ANEESLAANELAQASSAAAAEAEAKANAGREAAAAALAIAEAAVAIEQEAVILARKAQDARLNAEAAAAA
AMNARVIASAESEASEDLENRASVARASAAGAAEAKAIATDAGATAEIAAYSWAKKGELINPGPLPKIIS
VNADLSKSEVEAMKITRGQVQEVKKISTHKGGWGWGKEGRSKVSSNASARASASANAAAGSLGSKWGRQL
SASSASADANAEADSQLLKVW

#### GAF1 (SEQ ID NO:57)

MKIPAIIATTLLLWGFADASKSYLLGSSASASASASASAGGSTGGVGVGSVISGGNNIIRGASTTSVT LAAAABAKAALNAGKATVEEQREALQLLTASAEKNAEARSLADDAAVLVQGAAEAQSVAAAKTVAVEQG SNSLDAAAAEALAAAASRVSAQQALQAAQTSAAAIQTAAGSALTALKLARKQEAESNNAAEQANKALAL SRAASAATQRAVAAQNAAAASAASAGAAQAEARNAYAKAKAAIAALTAAQRNYAAAKASASAGSVVAEQD AQSRAADAEVNAVAQAAARASVRNOEIVEIGAEFGNASGGVISTCTRSSGGRGVSVTAGAQASASASATS SSSSSSGINKGHPRWGHNWGLGSSEASANAEAESSASSYSS\*

#### GAF2 (SEQ ID NO:59)

MKIPAIFVTSLLAWGLASGGVIGPDTSSSSQASASASASASASASASASIGYNELHKSINAPALAVGVKN GGVDVAKGAAVVESAISDVSTLTDDRTINGLAIIGNSABSLARAQASSASAGAKANALIKQSIAAIEIT EKAEYLASIVATKAAKAAEATAAATARATAVAEAAKVSSEQFAAEARAAADAEAKANAASIIANKANAVL AEAATGLSASAGKAQQSATRALQAARAAAKAQAELTQKAAQILVLLAEAKAAVSRASADQSVCTSQAQAA SQIQSRASAAESSASAQGEANTIAAEAVARADAEAASQAQAWAESFKRELSSVVLEAEANASASASAGAL ASGSSSSGASSSADASAGASSYGSLGGYRHGGSFSEASAAASAASRAEAA

#### GAF3 (SEQ ID NO:61)

MKIPAILVTSFLAWGLASGGVPKELGTSISSASASASASASATASSSSKNVHLLPLKSEHGIVIDKSKFN IRKVVLSAIDEINGAPNIGLGLKQVSLALAKAQASAQSSAEALAIIKKIVALLISAYVRAAEAARRASAE ALATVRAAEQAQKTAEAKGRAAEALSELVEASQKADAAAAGTTDAIERTYQDARAATSAQTKASCEAEN ANRNAAATLAAVLSIAKAASQQGTRAAVDAAAAAAAAAAAHAKANAVSQATSKAAAEARVAAEEAASAQ ASASASAQLTAQLEEKVSADQQAASASTDTSAAIAEAEAAALASTVNAINDGVVIGLGNTASGSAQASAQ ASALARAKNARPRIKGWYMIGGATSASASASASASASOGSOGLVY

#### GAF4 (SEQ ID NO:63)

#### MalF1 (SEQ ID NO:73)

Figure 10 continued

#### Xenospiral (SEQ ID NO:12)

#### Xenospira2 (SEQ ID NO:14)

#### Xenospira3 (SEQ ID NO:16)

#### Xenospira4 (SEQ ID NO:18)

Figure 11

#### Xenosin (SEQ ID NO:20)

#### BBF1 (SEQ ID NO:32)

#### BBF2 (SEQ ID NO:34)

#### BBF3 (SEQ ID NO:36)

Figure 11 continued

ACCGCAGCCGCAGCTGTCGGAGATGGAGCTATTATAGGACTTGCACGGGACGCTAGTGCCGCAGCTCAGGCAGCCGCAGAGTTAAAGCCTTAGCTGAAGCTAGTGCCAGCTTAGGTGCTTCAGAAAAGGACAAGAAATGA

#### BBF4 (SEO ID NO:38)

#### BBSA1 (partial) (SEQ ID NO:39)

GGAAATTCGGAAAGCGGCGAAAATTGGAAGAACGGTGAAAGCTCCGAAAGCGGCAAAAATTGGAGGAACAGCGGAAGC agcggcgagaatggaaaacagtgaaagctccgaaagcggcaaaaattggaagaacagcggaagctccgaaagcggc TGGAAAACAGTGAAAGUGGAAATAAAGGCAAAAGCTCAAAAAGCAGCGAAAGTTGGAAGAGCAACGAAAACTCGAAG AACGACGCCAGCTGGAAGAGCAGTGAAGAATCAGAAAAGTGGAAAGATGGTAAAGCAGTGGCGGAAGACAGCGTTAGT ATABACTGGGCAGATGTCAAAGAGCAGATTAGCAACATTGCTACATCCTTAGAAAAGGGTGGTAACCTCGAGGCTGTA  $\tt TTGAAAATAAAGAAAGGAAAAGAAAATTTCAAGTTTGGAGGAAATCAAGGAGAAAATCTCTGTCCTACTGAAATGG$ GGCAAAGTAATTTTAGAATTGCAAAGCGCCATAGAAAAGGTTCTCGTAAAGTCAGAAAAGGTAACCAAAGTATCTGAA GTTTCCGGTTTAGTAAAAAGCAAAACTGTCTCGGACATAAAACCGCTTCAAGCAGTAATTCCTTTAATCCTTGAATTG CAAAAAACAGACATTAACCTTAGTACCTTAAACAACTGGTCCACTGTTAACGTAAATTCTATAGATAAAGAACGCGTC ACGAAAACGGTTCCAGTGCTCCTTCAATCCATGAAAGGAGGCGAAGATATTCAGAACCTTTTGAGTGCGAAAGGTGCA GGTGCGTTGAACTCAAAAGGCTTGTTGAACTTGAAAGACGGCGCTAGTGTGTTAGGTGCAGGAAAAATCGGAGGATTA ATTCCTT"ACCGAAACTTTAAGAGATAGACCGATAAAGGCAGATATACTCTCGGAAGATTTTTTTGGAAGTTGAATAG TAAATAA

# BAF1 (SEQ ID NO:49)

ATGAAGATCCCAGCGATAATCGCAACGTCCCTTCTCCTCTGGGGTTTCGCCAGCGCCCAGCGGCCCCCCTTACTCGGC GGCAGATCGGCGGGTCGGCTTCGGCTTCGGCTGAGGGGTCGGCGGGGGTTGGAGGAAAAGCGGCGCATCC GCTTCCGCTTCCGCTAAGGCTGGTAGCAGCAACATCCTCAGCCGCGTGGGAGCTTCGAGGGCGGCGCGACGTTGGTC GCTTCCGCCGCGGTGGAGGCCAAGGCGGGTCTCCGTGCCGCAAGGCAACCGCCGAGGAGCAGAGGAGGAGGCTTTGGAA ATGCTCACCTTGTCCGCCGACAAGAATGCCGAGGCGCGTATCCTGGCCGACGACGACACGCCGTTCTGGTTCAAGGCAGC GCCGAGGCACAGTCGCTCGCCGCGAAGACCGTCGCGGTCGAGGAAGAGTCCGCTTCCTTGGATGCGCCGCAGTT GAAGCGGAGGTCGCAGCCGCCACGTCGAAATCGTCGGCTGGCCAAGCACTCCAGTCCGCACAGACCGCCGCATCTGCT CTCAGAACTTCCGCCAGGAGCGCCTTGACGGCCCTCAAGCTGGCACGCCTCCAAGGCGCGCTTCTAGCAACGCTGCC AGGATGATAGGAAAAGGCCTGGCCGCCACCAGCACGCAAATGCCGCCCCACAAGCTATGCCGCCGAGAGTGCA GCCGCAGAAGCAGCGGCTATCGCGGCAGCGAAACAATCGGAGGCGAGAGACGCCGGCGCCCGAGGCCAAGGCCGCCATG GCAGCACTCATCACCGCCCAGAGGAATCTCGTGCAGGCCAATGCCAGGGGGGAAATGGCAAGCGAGGAAGCCGAATTG GATTCGAAGTCTAGAGCGTCCGACGCCAAGGTGAACGCCGTTGCTCGTGCGGCCTCCAAGTCCAGCATACGCAGAGAT Caagacgccatcgccaccgccgaggcatcgagtaecgcgtccgccgtcggcatcaagaaaacaagcggacactgggg AGCGGAAAATGGAGTCGTGTCTCCAAGGGTAAAGGATGGGCTTCCTCGAATGCGGACGCTGACGCCAGCAGCAGCAGCAGC GCCGGCACACTCCTGCTGTAA

Figure 11 continued

#### BAF2 (SEQ ID NO:51)

ATGAAGATTCCAGCGATACTCGTGACGTCTCTCCTCGCCTGGGGATTAGCCAGCGGCCGGGTCATCGAGTCCAGCTCG GGCAAGGAGGAGAAACTCGAAGAACTCGACGAGGAATCGCTCAATGAGGCCGCTCTGAAGGTCGGCATCAAGAAC GGCGGATTGGATGTCGCGAAGGGCGCGGCAGTCCTCGAGGCAGCGATGAGCGACCCTTACGGATCAGCGT TCTCTTGTGGATCTCGGTCTCGGCCGGTCGCGAACGAGGCCGAGAFCCTGGCGAGGCCGCAACGCCCACGAGCGCC CAAGCTGGCGCTGTCGCTAATAGCGCCGCGGAGCGTGCGATCGCGGCGATGGAGATGGCCGACAGAACCGAATATATT tcagcctccaagatatccagtcaggaatcagccgcatcggccgctaacgccGCCaacgccgaagccaaggccaacgcc GCTTCCATAATCGCTAACAAGGCGAACGCCGTCCTGGCTGAGGCCGCCGCCGTACTCGCAGCCACTGCTACCAAGGCC AAGGAATCGGCGATGAAATCGCTTAGCGCCGCTCAGGCCGCCGAAGGCACAAGCCAGGAACGCCGAGGCCTCCGCC GAAGCTCAGATCAAACTTTCCCAGGCCAGGGCCGCGTGGCACGCGCTGCAGCCGATCAGGCCGTCTGTTCCTCCCaG GCTCAGGCCGCAAGTCAGATACAATCGAGGGCATCCGCATCCGAATCCGCGCATCGGCACAATCAGAGACCAACACC GCCGCGCCGAAGCGGTCGCCACCGCTGACGCCGAAGCGGCCGCGCAAGCTGAAGCGTGGGTCATGTCGCTGAAGAAC GATCTGTGGCTGCATCTCAACATGAAGGGTGAGGCCAAGGCCGAAGGCGAGGCCGTTTCGATCAGCAAAGGACATCGC GGCGGTATCAGGTCGGGCAGCATCTCGGAAGCCAGCGCCGAGGCAAGCAGCACGTTTCCATGGGCGGACGTCATGGA CGGAAGGACCTCGTCTCTGAAGCGTTAGCGGGGGGCATCAGCGGGCAGCAGTGCCGACTCCCTTTGA

#### BAF3 (SEQ ID NO:53)

atgaagataccagcgatactcgtgacgtccttcctcgcctggggactggccagcggaatctcccttaaggagtcgaaa GCTTCCGCGTCCGCGTCCGCGTCCGCTTCCGCGAGGGCCCAGCGCAAGAAGAATCTTCACGTGTTGCCATTACCGAAG AAAAGCGAGCATGGCATCGTGATCGACAAGTCGGTGTTCGACATCAAGGATGTAGTGCTGAGCGCGGTCGACGAGATC AACGGCGCCCGAAACTCGGCCTGGGATGGAAGAAGGTCAGCATGGGGGTGGAGCGCCGAGGCGAACGCAGCCGCT GCCGCCGAGGCATTGGCGATGATCAAGAAGATTGCCATGGCCCGCAGCAGTGCATACGTCCAGGCGGCCTGGGCATCG GCCCAGGCATCAGCTGACGCATTGGCTAGCGCCAGGGTGGCACAGGCGTCTCAGGAGGCTGCGGAGGCAAAGGGTAGA ecgettccgaggcgettccagagccatcgaagcatcctcgcgagccgatgcgccaccgctgcgacgctggacgcg atggaccgcaccatggagaacgcgagggcggcaaatgccgcgaaacgcaggccagcggccaagctgaagcgcaaat CGCAGCGCTGCTGCCATCCTCGCAGCTCTGCTACGTATCGCGGAGGCATCCGCGTTGAACAACGACGACGCCGCTCAAC GCGGCGCGCGCAGCCGCAGCGTCTGCCCTTCAGGCCAAGGCTAACGCGGCTTCTCAAGCAACCGCCAGAGCCGCA GGACAGGCGTCGACGGCCGCCAAGAGGCGCAATCCGCCCAAGAAGCCGCCGATAAGAACGCGGAGCTGACCACGGTC ATGCTCGAAAAGGCTAGTGCTGATCAACAGGCGGCATCCGCTAGGGCTGACTACTACACCGCCTCAACCGAGGCCGAA GCCGCTGCACAGGCGTCTGCTATCAACGCACTCAGGGACGGAATAGTTGTCGGAATGGGAAATGACGCTGGCGCATCG GCCCAGCGATGGCACAGGTAGAAGCTCTCGCTCGCGCCAGCGAGCACAAGGCGTTAGGCGAGAAGAAGAAGAAGGCCTG GTTTGGGGCTACGGAAGCAAGGGCAGTAGCTCCGCCAGCGCATCCGCCAGCGCCTCCGCCGAAGCATCCTCGAGACTC GGAAAGGACTGGTAG

#### BAF4 (SEQ ID NO:55)

AGTGCGCCGCCTCTGCGCAAGCGGAAGCGTCTCGTCTGTCGCTCGGCAAACTGTCCGCGTCTCAGGCTTCCGCC AAGAGCGAGGCGAAGAGCGCCGCCGCGATCGCGGTCGAAGGGCTAAAATCGGCACCGGAATCGGAAATACCGCGTCC GCATCCGCGGAGGCGCTCTCACGAGGACTCGGCATCGGACAGGCGGCGGGGGGGCGCAAGCCGCAGGCCGCAGGTCAG GCAGAGGTCGCCGCGAAATCGTGCGAACTTGCCGACAAGACCACCGCCAAAGCGGTCGCCATGGTCGAAGCGGCAGCC GAGGCCGAAATCGAGGTGGCCAATCAGGAGGTCGCAGCCGTCAAATTATCGACTTGGGCCGCTAAAGCAGCAGGATA GTCGAGGAAGACAGCGCCCCTGAGGGCGCCTGCCGCAAATTGCTTTTGGCCGCGAGAGCTGCCGCCGCCGCCGAG AAAGCGAACGCCGGCCGTGAGGCCGCTGCCGTTGGCTTTGGCTATCGCCGAGGCCGCCGTCGCCATCGAACAAGAAGACCC GTCATTTTGGCTCGCAAGGCACAAGATGCCCGTTTGAATGCTGAAGCCGCAGCCGCCGCTGCATGAACGCCCGTGTC ATCGCTTCCGCCGAATCCGAGGCCAGTGAAGATCTGGAGAATCGCGCTAGTGTGGCGCGGTGCCAGTGCCGGTGCC GCTGAGGCAAAGGCTATCGCCACCGATGCCGGCGCCACTGCCGAGATCGCGGCCTACAGTTGGGCCAAGAAGGGCGAA CTGATCAACCCCGGCCCGTTGCCGAAGATCATCAGCGTCAACGCCGATCTGTCCAAGAGCGAGGTCGAGGCCATGAAG GGAAGACAACTATCCGCATCATCCGCGTCGGCTGACGCCAACGCCGAAGCCCACAGCCAGTTGCTGAAAGTGTGGTGA

#### GAF1 (SEQ ID NO:65)

Figure 11 continued

#### GAF2 (SEO ID NO: 67)

ATGAAGATTCCAGCGATATTCGTGACGTCTCTGCTCGCCTGGGGACTCGCCAGCGGCGGAGTCATAGGTCCCGACACG TCCTCATCGTCCCAGGCATCGGCATCGGCCTCAGCATCGGCGTCGGCATCGTCGGCATCGGTAC AACGAACTCCATAAATCGATCAATGCGCCCGCCTTGGCGGTCGGCGTCAAGAACGGCGGAGTGGATGTCGCCAAGGGC GCGGCCGTTGTCGAaTCAGCGATATCCGACGTATCGACTCTAACCGATGATCGTACGTTCGACGGTCTCGCTATCATC GGGAATAGCGCCGAGAGTCTGGCAAGAGCACAGGCTTCCTCGAGCGCCAGCGCCGGCGCAAAAGCCAATGCTCTCATC AAACAATCGATAGCGGCTATAGAGATCACCGAAAAGGCAGAGTACCTTGCGTCGATCGTCGCCACCAAGGCAGCGAAG GTCCTCGCGGAGGCACCCGGACTTAGCGCCAGCGCTGGCAAAAGCCCAACAATCGGCGACCAGGGCGTTGCAAGCC GCACGAGCTGCCGCTAAGGCTCAAGCCGAACTTACCCAGAAAGCCGCTCAAATCTTAGTCCTCATTGCTGAAGCCAAA  ${\tt GCCGCCGTGAGCCGAGCAGCCGCCGATCAATCCGTCTGTACGTCCCAGGCACAAGCCGCCAGTCAGATTCAATCGAGA}$ GCCTCCGCGGCCGATCCGCCATCGGCTCAATCGGAAGCCAACACCATTGCGGCCGAGGCGGTCGCTAGAGCTGAC GCCGAGGCGACCAGTCAAGCTCAAGCGTGGGCCGAATCCTTCAAACGCGAACTCTCGAGTGTCGTTTTGGAGGCCGAG GCCAATGCCTCGGCTAGTGCCTCGGCTGGTGCCCTGGCCAGTGGTAGCAGCTCGGGCGCGAGTTCCAGCGCGGAT GCCAGCGCCGGAGCCAGCTATGGATCCTTGGGCGGATATCGACACGGCGGAAGCTTCAGCGAGGCATCGGCAGCC GCGTCAGCGGCCAGTCGCGCGAGGCTGCGTAA

#### GAF3 (SEC ID NO: 69)

ATGAAGATTCCAGCGATACTCGTGACGTCCTTCCTCGCCTGGGGACTGGCCAGCGGGGGTGTCCCTAAAGAGTTGGGA ACTTCCATTTCTTCCGCGTCCGCATCCGCATCCGCATCCGCACCGCGTCCTCCAGTAGCAAGAATGTTCAC  $\verb|THATTACCATTGAAAAGCGAGCATGGCATCGTAATTGACAAGTCAAAATTCAACATCAGAAAGGTAGTGTTGAGCGCA|$ ATCGATGAGATCAACGGCGCGCCCAACATCGGTCTGGGAITGAAACAGGTCAGTTTGGCGCTCGCAAAAGCCCAGGCT AGTGCTCAATCGAGCGCCGAGGCATTGGCAATCATCAAGAAAATCGTCGCGCTCCTCATCTCGGCCTACGTCAGAGCA GCCGAGCCCGCGCTCGAGCATCCGCCGAAGCTTTAGCTACCGTTAGGCCTCCGGAACAAGCGCAAAAAATTGCTGAA GCGAAGGGTAGAGCGGCTGCTGAGGCGCTCTCCGAGTTAGTCGAGGCGTCCCAGAAGGCCGATGCGGCGGCGGGGA ACGACGGACGCGATCGAACGCACCTACCAGGATGCCAGAGGCCACCTTCCGCACAGACCAAAGGCCAGCGGCGAAGCC GAGAATGCTAATCGCAATGCTGCCGCCACCCTCGCGGCGGTCTTTGAGCATCGCTAAGGCCGCCTCCGGTCAAGGAGGC ACTCGAGCCGCTGTCGATGCAGCTGCTGCCGCTGCCGCCGCAGCCGCTCTGCATGCTAAAGCTAACGCGGTTTCGCAA GCTACCAGCAGAGCCGCTGAAGCTAGAGTCGCGGCTGAGGAGGCATCCGCCCAGGCATCCGCCTCAGCAAGC GCACAGCTGACCGCACAATTAGAGGAGAAAGTCAGCGCCGATCAACAAGCAGCCTCCGCCAGTACTGATACCTCCGCT GCTATAGCCGAGGCTGAAGCTGCCGCGTTAGCGTCCACCGTCAACGCACACGACGGAGTGGTCATCGGATTAGGA AAGGGCTGGTACAAAATCGGAGGCGCGACTTCCGCTTCTGCAAGCGCATCGGCCAGCGCTTCCGCCCAGTCATCCTCG CAAGGACTGGTATACTAG

#### GAF4 (SEQ ID NO:71)

Figure 11 continued

ATCGCCCAAGCCGCCTTAACATCGAGCAAGAGCTGTTAAATTGACCCGCCAGGCCCAGAATACTCGTCTCAGATCT
GAAAATATTCTCGCCGGGGCCAGCAATGCCGGCCCATCGCTTCGCTTCAGGCCCAGGCCAGAATACTCGTCTCAGATCT
GCTGCGAATGCAGCGCTTCCAATGCCCGAGCCGCTCCGCCAGACCCGTAGCTACCCGAAGCCGCTTCTACCGCC
GAGATCGCAGCTTATACTTCATCCGAGAAAGGCGAGATCACCAATCCCGGTCCTCTGCCCAAGATCGTCAGTGTTACC
GCAGGTCTGACCCAGAACGAAATAGCGGGATCAGGACCGGCCGCTAGTGCCAGTGCCAGTGCCAGTGCCAGT
GCCGGTGCCGGTGCAGGTCCAGGAGCCGGTGCAAGTGCAGGAGCCGGTTCAGTGCCAGTTCCAGTGCCAGT
GCAGGAGCCGGTGCTACTGCCGGAGCGAGCTGCAGGAGCCGGTGCCAGCAGTTTACTCTTGCCGCAG
AGTAAACTCCATCCAATCTCCAGGTCTCCGCCTCTGCCTCCGCTTCCGCGAGGCCGAAGCTAACAGTTCGGCGTAT
GCGTAA

#### MalF1 (SEQ ID NO:75)

ATGGCAGCGTCGAACAAAATCATCTTCAGCTTTTTAGCTATTGTTCTATTACAACTTGCCACACACTGTTCATCAACA  $\tt GCTGTATTGATTTCTGGTTCGGCTGCTGCTTCCTCACACAATGCTGCTGCTGCAGCTGCAGCCAGAGCTGCC$ GCCGCCGCCGCTAGTGCTGCAGCTGCAGCTGCCAGACGAGCTGGCGCTATTGGCCTAAATGGAGCAGCTGGAGCTAAT  ${\tt GTAGCTGTCGCTGGCAAAAAAGGAGGTGCTGCTGGATTAAATGCTGGCGCTGGTGCTTCTTTAGTATCTGCAGCT}$ GCAAGACGAAATGGAGCCCTTGGACTTAACGGTGCAGCTGGAGCAAATCTCGCAGCAGCTGGTGGCAAAAAAGGAGGT GCTATTGGATTAAACGCTGGAGCATCAGCCAATGTTGGTGCCGCTGCTGCCAAGAAAAATGGAGCCATAGGACTTAAC TCAGCTGCTTCAGCTAATGCTGCCGCTGCCGCTGCTAAAAAAGGTGGAGCCATTGGATTGAATGCTGGAGCTTCAGCA AATGCTGCTGCCGCCGCCGCAGAAGAGGCTGCGGGGCTGTTGGATTAAATGCTGGAGCTTCTGCTAACGCTGCTGCTGCT GCTGCTGATGCCGCAAATGCTGCTGCTTCTGAAAGTGCTGCTGCTGCAGCCAAGAAAGCCGCCGCTGTTGCTGAA AATGCAGCTGCCACCGCCAATGCCGCTTCAGCTTTACGTAAAAATGCATTAGCCATTGCCAGTGATGCAGCAGCTGTC CGTGCTGATGCCGCTGCCGCCGCTGACGATGCTGCTAAAGCTAACAACGCTGCTTCCCGTGGAAGTGATGGTTTA ACTGCCGGGCCAATGCCGCCACTTTAGCCAGTGATGCTGCCCGTAGAGCTAGCAATGCAGCAACAGCTGCCAGCGAT GCTGCCACTGACCGATTGAACGCCGCCACCGCTGCTAGCAACGCTGCCACTGCTCGCAAATGCCGCCACACGTGCC GATGATGCCGCCACTGATGCCGACAATGCTGCTTCAAAGGCCAGTGATGTATCAGCTATTGAAGCCGACAACGCTGCA GCTGCCAATGCTGCTGATGCCGCTGCCCAATGTAATAACAAAGTTGCCCCAGTAAGTGATGCCTTAGCTCTCGCCGCT AATGCTGCCGGGGGGTCTGATGCCGCCGCTGAAGCTCAAGATGCTGTTGCCAGAGCAAGTGACGCTGCCGCTGCC CAAGCTGATGGTGTTGCCATTGCCGTAAATGGAGCTACTGCGAGAGACTCAGCAATTGAAGCCGCTGCTACTGCTGGA GCTGCCCAAGCTAAAGCCGCTGGACGTGCTGGAGCTGCTGCAGCTGGTTTAAGAGCTGGTGCCGCTAGAGGTGCTGCC GCTGGTAGTGCCCGCGGTCTAGCTGGAGGATTAGCTGCAGGTTCCAATGCTGGAATCGCGGCTGCTGCAGCTTCTGGA TTAGCAAGAGGCGCAGCTGCTGAAGTTTGCGCAGCTAGAATAGCATTGTAA

Figure 11 continued

#### Xenosin - Inclusion of intron

ATGAAATACATGCTCTTGTTGCTATCTATATTCATCTGTGCACATATTGTATGCGCAGGCGTAAATACAG AATTAAAAAAGATGGTGAACTAAAGGAAGAGTCTTATGAGAAAAGCGAGTCAAAGAGTTTAAAAGAAAT TAAAGAAGAACGTGCTTCAAAATCAAAAAGTGAACGTTTGAAGATTCGTGAAGGTAATTCGTGAGATTCA AGATTCAAATCAATTÄÄÄTTTGAAAATTATGAAAGTAGTÄTTGTTÄÄÄTTÄTÄAGATAGAAGATTTTTATC Taaaaaataataaattaagetttttgtatttttggätättgtagatatttttaatatagaattettatan TTAAAGTTCAAATTAAAAATTTGTAAAAAATATGGAAAAACATAAAAATTGAATTTGTTGTAATTTAAA AAGGATTTTTATTTATTGATTAATTATGAÄTATAAGTTCGAÄAAATCCTAAATATTAATGTTTÄAÄÄ AAAAATTAGGTTTTTAATTTTAAGAATCAAATGGTAAAAAACATTTTAAATTTGAAATATATAAAGTAA ÄTÖTTTTÄATCGACAAGGGÄTGAATTTATTGATTAGAAAAACGCGAAGAGAAAAAATCCAAGAGTC TCCTCTTTTGGAAGAAAAAATGGCAAAGGTCTATTGGGTTTTGGAAGATGTCACGGACGAGTTAAATATC GCTCTTAAATCGTTGAAGGAGGGCAAAAAGTTTGATACTTGGAAATTCGAGAAAGGTAGCGAAGACGTTC TGGTGCTATAGATTTGGAGAAGAATGGTAAGGTACTTGTAGATTTGGAAAAAATCTCAGAAAAACATACTT GAAACTTGTGGATCACAAAAGAAGACTGTGGAAGTTGTAGATGATAAAGACAAAAAATGGAATAAAGAAT TTTGCTTGGCGGTTTAAGTGGCCTCTTAAATAGTTTAAAATCAGAAAAAGGTCTTCTAGGTCTTTTGAAT AAGAATCAAATTGAGTTATTAATTCCTTTAATCAGTGAGATAAAAAAGAAAAATATAGATTTTAATCTCT TCGATTCTGTTGATTCTGTCGAAAGAAATTTAGACTTGAAACTTTTCACAAGTTCTGTTTCAAAAGTTAC TGAATTATTAAATAAAGGAATCGATATTCAAACAATTTTGAATGCGAAAAATGGAGATGAATTCGATTTA AGCGGCAAAGAATTGAAAAACGTCAAAGGGATATTTGGTTTGATTGGAAGTTTGAAACGCTCATTAGGAT TAGAAATATATTGAACTTACCGTTTAAACGTATACCTCTGCTTAAATTA

Figure 12

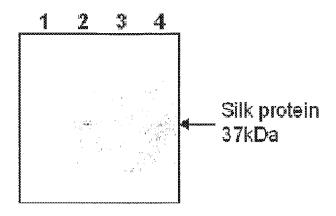


Figure 13

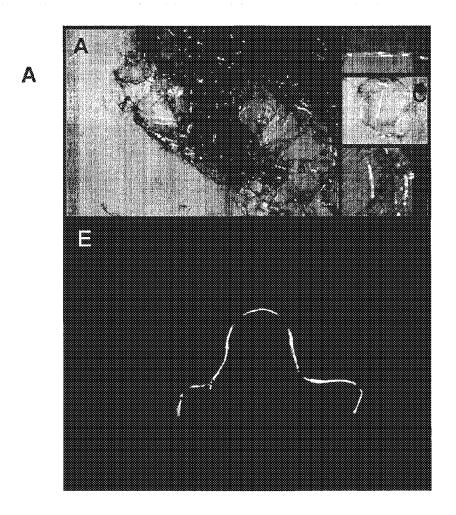


Figure 14

#### SILK PROTEINS

#### FIELD OF THE INVENTION

**[0001]** The present invention relates to silk proteins, as well as nucleic acids encoding such proteins. The present invention also relates to recombinant cells and/or organisms which synthesize silk proteins. Silk proteins of the invention can be used for a variety of purposes such as in the production of personal care products, plastics, textiles, and biomedical products.

# BACKGROUND OF THE INVENTION

[0002] Silks are fibrous protein secretions that exhibit exceptional strength and toughness and as such have been the target of extensive study. Silks are produced by over 30,000 species of spiders and by many insects. Very few of these silks have been characterised, with most research concentrating on the cocoon silk of the domesticated silkworm, *Bombyx mori* and on the dragline silk of the orbweaving spider *Nephila clavipes*.

[0003] In the Lepidoptera and spider, the fibroin silk genes code for proteins that are generally large with prominent hydrophilic terminal domains at either end spanning an extensive region of alternating hydrophobic and hydrophilic blocks (Bini et al., 2004). Generally these proteins comprise different combinations of crystalline arrays of  $\beta$ -pleated sheets loosely associated with  $\beta$ -sheets,  $\beta$ -spirals,  $\alpha$ -helices and amorphous regions (see Craig and Riekel, 2002 for review).

[0004] As silk fibres represent some of the strongest natural fibres known, they have been subject to extensive research in attempts to reproduce their synthesis. However, a recurrent problem with expression of Lepidopteran and spider fibroin genes has been low expression rates in various recombinant expression systems due to the combination of the repeating nucleotide motifs in the silk gene that lead to deleterious recombination events, the large gene size and the small number of codons used for each amino acid in the gene which leads to depletion of tRNA pools in the host cells. Recombinant expression leads to difficulties during translation such as translational pauses as a result of codon preferences and codon demands and extensive recombination rates leading to truncation of the genes. Shorter, less repetitive sequences would avoid many of the problems associated with silk gene expression to date.

[0005] In contrast to the extensive knowledge that has accumulated about the Lepidopteran (in particular the cocoon silk of *Bombyx mori*) and spider (in particular the dragline silk of *Nephila clavipes*) little is known about the chemical composition and molecular organisation of other insect silks.

[0006] In the early 1960s, the silk of the aculeate Hymenopteran was shown to have an alpha-helical structure by X-ray diffraction patterns obtained from silk fibres drawn from the salivary gland of honeybee larvae (Rudall, 1962). As well as demonstrating that this silk was helical, the patterns obtained were indicative of a coiled-coil system of alpha-helical chains (Atkins, 1967). Similar X-ray diffraction patterns have been obtained for cocoon silks from other *Aculeata* species including the wasp *Pseudopompilus humbolti* (Rudall, 1962) and the bumblebee, *Bombus lucorum* (Lucas and Rudall, 1967).

[0007] In contrast to the alpha-helical structure described in the Aculeata silks, the silks characterised from a related clade to the aculeata, the Ichneumonoidea, have parallel-β structures. X-ray diagrams for four examples of this structure have been described in the Braconidae (Cotesia(=Apenteles) glomerate; Cotesia(=Apenteles) gonoptervgis; Apenteles bignelli) and three in Ichneumonidae (Dusona sp.; Phytodietris sp.; Branchus femoralis) (Lucas and Rudall, 1967). In addition the sequence of a single Braconidae (Cotesia glomerate) silk has been described (Genbank database accession number AB 188680; Yamada et al., 2004). This partial protein sequence consists of a highly conserved 28 X-asparagine repeat (where X is alanine or serine) and is not predicted to contain coiled coil forming heptad repeats. Extensive analysis of the amino acid composition of the cocoon silks of the Braconidae has shown that the silks from the subfamily Microgastrinae are unique in their high asparagine and serine content (Lucas et al., 1960; Quicke et al., 2004). Related subfamilies produce silks with significantly different amino acid compositions suggesting that the Microgastrinae silks have evolved specifically in this subfamily (Yamada et al., 2004). The partial cDNA of Cotesia glomerata was isolated using PCR primers designed from sequence obtained from internal peptides derived from isolated cocoon silk proteins. The predicted amino acid composition of this partial sequence closely resembles the amino acid composition of the extensively washed silk from this species.

[0008] The structure of many of the silks within other non aculeate Apocrita and within the rest of the Hymenoptera (Symphata) are most commonly parallel- $\beta$  sheets, with both collagen-like and polyglycine silks produced by the Tenthredinidae (Lucas and Rudall, 1967).

[0009] Honeybee silk proteins are synthesised in the middle of the final instar and can be imaged as a mix of depolymerised silk proteins (Silva-Zacarin et al., 2003). As the instar progresses, water is removed from the gland and dehydration results in the polymerisation of the silk protein to form well-organised and insoluble silk filaments labelled tactoids (Silva-Zacarin et al., 2003). Progressive dehydration leads to further reorganisation of the tactoids (Silva-Zacarin et al., 2003) and possibly new inter-filamentary bonding between filaments (Rudall, 1962). Electron microscope images of fibrils isolated from the honeybee silk gland show structures of approximately 20-25 angstroms diameter (Flower and Kenchington, 1967). This value is consistent with three-, four-, or five-stranded coiled coils.

[0010] The amino acid composition of the silks of various aculeate Hymenopteran species was determined by Lucas and Rudall (1967) and found to contain high contents of alanine, serine, the acid residues, aspartic acid and glutamic acids, and reduced amounts of glycine in comparison to classical fibroins. It was considered that the helical content of the aculeate Hymenoptera silk was a consequence of a reduced glycine content and increased content of acidic residues (Rudall and Kenchington, 1971).

[0011] Little is known about the larval silk of the lacewings (Order: Neuroptera). The cocoon is comprised of two layers, an inner solid layer and an outer fibrous layer. Previously the cocoon was described as being comprised of a cuticulin silk (Rudall and Kenchington, 1971), a description that only related to the inner solid layer. LaMunyon (1988) described a substance excreted from the malphigian tubules that made up the outer fibres. After deposition of this

layer, the solid inner wall was constructed from secretions from the epithelial cells in the highly villous lumen (LaMunyon, 1988).

[0012] It is also known that lacewing larva produce a proteinaceous adhesive substance from the malpighian tubules throughout all instars to stick the larvae to substrates, to glue items of camouflage on to the larvae's back or to entrap prey (Speilger, 1962). In the genus *Lomamyia* (Bethothidae), the larvae produce the silk and adhesive substance at the same time and it has been postulated that these two substances may well be the same product (Speilger, 1962). The adhesive secretion is highly soluble and is also thought to be associated with defense against predators (LaMunyon & Adams, 1987).

[0013] Considering the unique properties of silks produced by insects such as Hymenopterans and Neuropterans, there is a need for the identification of novel nucleic acids encoding silk proteins from these organisms.

#### SUMMARY OF THE INVENTION

[0014] The present inventors have identified numerous silk proteins from insects. These silk proteins are surprisingly different to other known silk proteins in their primary sequence, secondary structure and/or amino acid content.

[0015] Thus, in a first aspect the present invention provides a substantially purified and/or recombinant silk polypeptide, wherein at least a portion of the polypeptide has a coiled coil structure.

[0016] As known in the art, coiled coil structures of polypeptides are characterized by heptad repeats represented by the consensus sequence (abcdefg),, with generally hydrophobic residues in position a and d, and generally polar residues at the remaining positions. Surprisingly, the heptads of the polypeptides of the present invention have a novel composition when viewed collectively—with an unusually high abundance of alanine in the 'hydrophobic' heptad positions a and d. Additionally, there are high levels of small polar residues in these positions. Furthermore, the e position also has high levels of alanine and small hydrophobic residues.

[0017] Accordingly, in a particularly preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 10 copies of the heptad sequence abcdefg, and at least 25% of the amino acids at positions a and d are alanine residues.

[0018] In a further preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 10 copies of the heptad sequence abcdefg, and at least 25% of the amino acids at positions a, d and e are alanine residues.

[0019] In a further preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 10 copies of the heptad sequence abcdefg, and at least 25% of the amino acids at position a are alanine residues. [0020] In a further preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 10 copies of the heptad sequence abcdefg, and at least 25% of the amino acids at position d are alanine residues.

[0021] In a further preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 10 copies of the heptad sequence abcdefg, and at least 25% of the amino acids at position e are alanine residues.

[0022] In a particularly preferred embodiment, the at least 10 copies of the heptad sequence are contiguous.

[0023] In a further preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 5 copies of the heptad sequence abcdefg, and at least 15% of the amino acids at positions a and d are alanine residues.

[0024] In a further preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 5 copies of the heptad sequence abcdefg, and at least 15% of the amino acids at positions a, d and e are alanine residues.

[0025] In a further preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 5 copies of the heptad sequence abcdefg, and at least 15% of the amino acids at position a are alanine residues.

[0026] In a further preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 5 copies of the heptad sequence abcdefg, and at least 15% of the amino acids at position d are alanine residues.

[0027] In a further preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 5 copies of the heptad sequence abcdefg, and at least 15% of the amino acids at position e are alanine residues.

[0028] In a particularly preferred embodiment, the at least 5 copies of the heptad sequence are contiguous.

[0029] In one embodiment, the polypeptide comprises a sequence selected from:

[0030] i) an amino acid sequence as provided in any one of SEQ ID NO: 1, SEQ ID NO:2, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:56, and SEQ ID NO:57;

[0031] ii) an amino acid sequence which is at least 30% identical to any one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:56, and SEQ ID NO:57; and [0032] iii) a biologically active fragment of i) or ii).

[0033] In another embodiment, the polypeptide comprises a sequence selected from:

[0034] i) an amino acid sequence as provided in any one of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:58, and SEQ ID NO:59;

[0035] ii) an amino acid sequence which is at least 30% identical to any one or more of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:58, and SEQ ID NO:59; and [0036] iii) a biologically active fragment of i) or ii).

[0037] In another embodiment, the polypeptide comprises a sequence selected from:

[0038] i) an amino acid sequence as provided in any one of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:60, and SEQ ID NO:61;

[0039] ii) an amino acid sequence which is at least 30% identical to any one or more of SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:60, and SEQ ID NO:61; and [0040] iii) a biologically active fragment of i) or ii).

[0041] In another embodiment, the polypeptide comprises a sequence selected from:

[0042] i) an amino acid sequence as provided in any one of SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:62, and SEQ ID NO:63;

[0043] ii) an amino acid sequence which is at least 30% identical to any one or more of SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:62, and SEQ ID NO:63; and

[0044] iii) a biologically active fragment of i) or ii).

[0045] In a further embodiment, the polypeptide comprises a sequence selected from:

[0046] i) an amino acid sequence as provided in SEQ ID NO:72 or SEO ID NO:73;

[0047] ii) an amino acid sequence which is at least 30% identical to SEQ ID NO:72 and/or SEQ ID NO:73; and

[0048] iii) a biologically active fragment of i) or ii).

[0049] Further silk proteins which co-associate with proteins of the first aspect have been identified. One of these proteins (SEQ ID NO:10) is predicted to have 41% alphahelical, 8% beta-sheet and 50% loop secondary structure by PROFsec, and therefore is classified as a mixed structure protein. MARCOIL analysis of this protein predicted only a short region of heptad repeats characteristic of proteins with a coiled coil structure.

[0050] Accordingly, in a second aspect, the present invention provides a substantially purified and/or recombinant silk polypeptide which comprises a sequence selected from:

[0051] i) an amino acid sequence as provided in any one of SEQ ID NO:9, SEQ ID NO:10 and SEQ ID NO:30;

[0052] ii) an amino acid sequence which is at least 30% identical to any one or more of SEQ ID NO:9, SEQ ID NO:10 and SEQ ID NO:30; and

[0053] iii) a biologically active fragment of i) or ii).

[0054] Without wishing to be limited by theory, it appears that four proteins of the first aspect become intertwined to form a bundle with helical axes almost parallel to each other, and this bundle extends axially into a fibril. Furthermore, it is predicted that in at least some species such as the honeybee and bumblebee the proteins of the second aspect act as a "glue" assisting in binding various bundles of coiled coil proteins of the first aspect together to form a fibrous protein complex. However, silk fibers and copolymers can still be formed without a polypeptide of second aspect.

[0055] In a preferred embodiment, a polypeptide of the invention can be purified from, or is a mutant of a polypeptide purified from, a species of Hymenoptera or Neuroptera. Preferably, the species of Hymenoptera is *Apis mellifera*, *Oecophylla smaragdina*, *Myrmecia foricata* or *Bombus terrestris*. Preferably, the species of Neuroptera is *Mallada signata*.

[0056] In another aspect, the present invention provides a polypeptide of the invention fused to at least one other polypeptide.

[0057] In a preferred embodiment, the at least one other polypeptide is selected from the group consisting of: a polypeptide that enhances the stability of a polypeptide of the present invention, a polypeptide that assists in the purification of the fusion protein, and a polypeptide which assists in the polypeptide of the invention being secreted from a cell (for example secreted from a plant cell).

[0058] In another aspect, the present invention provides an isolated and/or exogenous polynucleotide which encodes a silk polypeptide, wherein at least a portion of the polypeptide has a coiled coil structure.

[0059] In one embodiment, the polynucleotide comprises a sequence selected from:

[0060] i) a sequence of nucleotides as provided in any one of SEQ ID NO: 11, SEQ ID NO:12, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:64, and SEQ ID NO:65;

[0061] ii) a sequence of nucleotides encoding a polypeptide of the invention,

[0062] iii) a sequence of nucleotides which is at least 30% identical to any one or more of SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:64, and SEQ ID NO:65, and [0063] iv) a sequence which hybridizes to any one of i) to iii) under stringent conditions.

[0064] In another embodiment, the polynucleotide comprises a sequence selected from:

[0065] i) a sequence of nucleotides as provided in any one of SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:66, and SEQ ID NO:67;

[0066] ii) a sequence of nucleotides encoding a polypeptide of the invention,

[0067] iii) a sequence of nucleotides which is at least 30% identical to any one or more of SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:66, and SEQ ID NO:67, and [0068] iv) a sequence which hybridizes to any one of i) to iii) under stringent conditions.

[0069] In another embodiment, the polynucleotide comprises a sequence selected from:

[0070] i) a sequence of nucleotides as provided in any one of SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:68, and SEQ ID NO:69;

[0071] ii) a sequence of nucleotides encoding a polypeptide of the invention,

[0072] iii) a sequence of nucleotides which is at least 30% identical to any one or more of SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:68, and SEQ ID NO:69, and [0073] iv) a sequence which hybridizes to any one of i) to iii) under stringent conditions.

[0074] In a further embodiment, the polynucleotide comprises a sequence selected from:

[0075] i) a sequence of nucleotides as provided in any one of SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:70, SEQ ID NO:71 and SEQ ID NO:76;

[0076] ii) a sequence of nucleotides encoding a polypeptide of the invention,

[0077] iii) a sequence of nucleotides which is at least 30% identical to any one or more of SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:70, SEQ ID NO:71 and SEQ ID NO:76, and

[0078] iv) a sequence which hybridizes to any one of i) to iii) under stringent conditions.

[0079] In another embodiment, the polynucleotide comprises a sequence selected from:

[0080] i) a sequence of nucleotides as provided in SEQ ID NO:74 or SEQ ID NO:75;

[0081] ii) a sequence of nucleotides encoding a polypeptide of the invention,

[0082] iii) a sequence of nucleotides which is at least 30% identical to SEQ ID NO:74 and/or SEQ ID NO:75, and

[0083] iv) a sequence which hybridizes to any one of i) to iii) under stringent conditions.

[0084] In a further aspect, the present invention provides an isolated and/or exogenous polynucleotide, the polynucleotide comprising a sequence selected from:

[0085] i) a sequence of nucleotides as provided in any one of SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, and SEQ ID NO:39;

[0086] ii) a sequence of nucleotides encoding a polypeptide of the invention,

[0087] iii) a sequence of nucleotides which is at least 30% identical to any one or more of SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, and SEQ ID NO:39, and

[0088] iv) a sequence which hybridizes to any one of i) to iii) under stringent conditions.

[0089] In a preferred embodiment, a polynucleotide can be isolated from, or is a mutant of a polynucleotide isolated from, a species of Hymenoptera or Neuroptera. Preferably, the species of Hymenoptera is *Apis mellifera*, *Oecophylla smaragdina*, *Myrmecia foricata* or *Bombus terrestris*. Preferably, the species of Neuroptera is *Mallada signata*.

[0090] In a further aspect, the present invention provides a vector comprising at least one polynucleotide of the invention.

[0091] Preferably, the vector is an expression vector.

[0092] In another aspect, the present invention provides a host cell comprising at least one polynucleotide of the invention, and/or at least one vector of the invention.

[0093] The host cell can be any type of cell. Examples include, but are not limited to, a bacterial, yeast or plant cell.

[0094] Also provided is a process for preparing a polypeptide according to the invention, the process comprising cultivating a host cell of the invention, or a vector of the invention, under conditions which allow expression of the polynucleotide encoding the polypeptide, and recovering the expressed polypeptide.

[0095] It is envisaged that transgenic plants will be particularly useful for the production of polypeptides of the invention. Thus, in yet another aspect, the present provides a transgenic plant comprising an exogenous polynucleotide, the polynucleotide encoding at least one polypeptide of the invention.

[0096] In another aspect, the present invention provides a transgenic non-human animal comprising an exogenous polynucleotide, the polynucleotide encoding at least one polypeptide of the invention.

[0097] In yet another aspect, the present invention provides an antibody which specifically binds a polypeptide of the invention.

[0098] In a further aspect, the present invention provides a silk fiber comprising at least one polypeptide of the invention.

[0099] Preferably, the polypeptide is a recombinant polypeptide.

[0100] In an embodiment, at least some of the polypeptides are crosslinked. In an embodiment, at least some of the lysine residues of the polypeptides are crosslinked.

[0101] In another aspect, the present invention provides a copolymer comprising at least two polypeptides of the invention.

[0102] Preferably, the polypeptides are recombinant polypeptides.

[0103] In an embodiment, the copolymer comprises at least four different polypeptide of the first aspect. In another embodiment, the copolymer further comprises a polypeptide of the second aspect.

[0104] In an embodiment, at least some of the polypeptides are crosslinked. In an embodiment, at least some of the lysine residues of the polypeptides are crosslinked.

[0105] As the skilled addressee will appreciate, the polypeptides of the invention have a wide variety of uses as is known in the art for other types of silk proteins. Thus, in a further aspect, the present invention provides a product comprising at least one polypeptide of the invention, a silk fiber of the invention and/or a copolymer of the invention.

[0106] Examples of products include, but are not limited to, personal care products, textiles, plastics, and biomedical products.

[0107] In yet a further aspect, the present invention provides a composition comprising at least one polypeptide of the invention, a silk fiber of the invention and/or a copolymer of the invention, and one or more acceptable carriers.

[0108] In one embodiment, the composition further comprises a drug.

[0109] In another embodiment, the composition is used as a medicine, in a medical device or a cosmetic.

[0110] In another aspect, the present invention provides a composition comprising at least one polynucleotide of the invention, and one or more acceptable carriers.

[0111] In a preferred embodiment, a composition, silk fiber, copolymer and/or product of the invention does not comprise a royal jelly protein produced by an insect.

[0112] In a further aspect, the present invention provides a method of treating or preventing a disease, the method comprising administering a composition comprising a drug for treating or preventing the disease and a pharmaceutically acceptable carrier, wherein the pharmaceutically acceptable carrier is selected from at least one polypeptide of the invention, a silk fiber of the invention and/or a copolymer of the invention.

[0113] In yet another aspect, the present invention provides for the use of at least one polypeptide of the invention, a silk fiber of the invention and/or a copolymer of the invention, and a drug, for the manufacture of a medicament for treating or preventing a disease.

[0114] In a further aspect, the present invention provides a kit comprising at least one polypeptide of the invention, at least one polynucleotide of the invention, at least one vector of the invention, at least one silk fiber of the invention and/or a copolymer of the invention.

[0115] Preferably, the kit further comprises information and/or instructions for use of the kit.

[0116] As will be apparent, preferred features and characteristics of one aspect of the invention are applicable to many other aspects of the invention.

[0117] Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

[0118] The invention is hereinafter described by way of the following non-limiting Examples and with reference to the accompanying figures.

# BRIEF DESCRIPTION OF THE ACCOMPANYING DRAWINGS

[0119] FIG. 1. Fourier transform infrared spectra of the amide I and II regions of the silks: 1) honeybee silk, 2) bumblebee silk, 3) bulldog ant silk, 4) weaver ant silk 5) lacewing larval silk. All the silks have spectra expected of helical proteins. The Hymenopteran silks (ants and bees) have spectral maxima at 1645-1646 cm<sup>-1</sup> (labelled), shifted approximately 10 cm<sup>-1</sup> lower than a classical alpha-helical signal and broadened, as is typical of coiled-coil proteins (Heimburg et al., 1999).

[0120] FIG. 2. Comparison of amino acid composition of SDS washed honeybee brood comb silk with amino acid composition of Xenospira proteins (namely, Xenospira1, Xenospira2, Xenospira3 and Xenospira4) (equimolar amounts totaling 65%) and Xenosin (35%).

[0121] FIG. 3. Comparison of amino acid composition of silk with amino acid composition predicted from proteins encoded by silk genes.

[0122] FIG. 4. Prediction of coiled coil regions in honeybee silk proteins. COILS is a program that compares a sequence to a database of known parallel two-stranded coiled-coils and derives a similarity score. By comparing this score to the distribution of scores in globular and coiled-coil proteins, the program then calculates the probability that the sequence will adopt a coiled-coil conformation as described in Lupas et al. (1991). Using a window size of 28 this program predicts the following numbers of residues exist in each protein in coiled coil domains: Xenospira3: 77; Xenospira4: 35; Xenospira1: 28; Xenospira2: 80. [0123] FIG. 5. Alignment of honey bee silk proteins showing MARCOIL prediction of major heptads that form

showing MARCOIL prediction of major heptads that form a coiled-coil structure. Heptad sequences are shown above the amino acids, and alanine residues in positions a and d are highlighted.

**[0124]** FIG. 6. Alignment of Marciol predicted coiled coil regions of hymenopteran (bees and ants) silk proteins showing the heptad position assignment. Amel, honeybee; BB, bumblebee; BA, bulldog ant; WA, weaver ant; F1-4, silk fibroins 1-4. Heptad sequences are shown above the amino acids, and alanine residues in positions a, d and e are highlighted.

[0125] FIG. 7. The amino acid character of heptad positions in the predicted coiled coil regions of the *Mallada signata* larval silk protein and the orthologous clusters of the Hymenopteran silk proteins.

[0126] FIG. 8. SDS polyacrylamide gel electrophoresis of late last instar salivary gland proteins. Proteins were identified after tryptic digest and analysis of mass spectral data set using Agilent's Spectrum Mill software to match the data with predictions of protein sequences from proteins identified from cDNA sequences. The software generated scores for the quality of each match between experimentally observed sets of masses of fragments of peptides and the predictions of fragments that might be generated according to the sequences of proteins in a provided database. All the sequence matches shown here received scores greater than 20 by the Spectrum Mill software, where a score of 20 would be sufficient for automatic, confident acceptance of a valid match.

[0127] FIG. 9. Parsimony analysis of the coiled coil region of silk proteins. The relatedness of the four coiled-coil proteins suggests that the genes evolved from a common ancestor predating the divergence of the Euaculeata. The

area bound by the dashed line indicates variation that occurred before the ants and wasps (Vespoidea) diverged from the bees (Apoidea) in the Late Jurassic (155 myrs; Grimaldi and Engel, 2005). Numbers indicating bootstrap values from 1000 iterations are shown.

[0128] FIG. 10. A) Apis mellifera silk proteins identified by mass spectral analysis of peptides generated from bee silk after digestion with trypsin. Shading indicates peptides identified by the mass spectral analysis. All the sequence matches shown here received scores greater than 20 by the Spectrum Mill software, where a score of 20 would be sufficient for automatic, confident acceptance of a valid match.

[0129] B) Full length amino sequences of bumblebee, bulldog ant, weaver and lacewing silk proteins.

[0130] FIG. 11. Open reading frames encoding honeybee, bumblebee, bulldog ant, weaver ant and lacewing silk proteins.

[0131] FIG. 12. Sequence of gene encoding Xenosin. Entire coding sequence provided which is interrupted by a single intron (highlighted).

[0132] FIG. 13. Expression of silk protein in tobacco. Detection of histidine tagged proteins after western blot analysis of proteins from: 1. *E. coli* transformed with empty expression vector, 2. *E. coli* transformed with expression vector containing AmelF4 (Xenospira4) coding region, 3. tobacco transformed with empty expression vector, 4. tobacco transformed with expression vector containing AmelF4 coding region.

[0133] FIG. 14. Fibres made from recombinant honeybee silk proteins showing birefringent threads. Birefringence indicates structure is present in the threads. Different recombinant honeybee threads are shown in each panel A-D, and recombinant lacewing thread is shown in panel E.

### KEY TO THE SEQUENCE LISTING

[0134] SEQ ID NO:1—Honeybee silk protein termed herein Xenospira1 (also termed herein AmelF1) (minus signal peptide).

SEQ ID NO:2—Honeybee silk protein termed herein Xenospira 1.

SEQ ID NO:3—Honeybee silk protein termed herein Xenospira2 (also termed herein AmelF2) (minus signal peptide). SEQ ID NO:4—Honeybee silk protein termed herein Xenospira2.

SEQ ID NO:5—Honeybee silk protein termed herein Xenospira3 (also termed herein AmelF3) (minus signal peptide). SEQ ID NO:6—Honeybee silk protein termed herein Xenospira3.

SEQ ID NO:7—Honeybee silk protein termed herein Xenospira4 (also termed herein AmelF4) (minus signal peptide). SEQ ID NO:8—Honeybee silk protein termed herein Xenospira4.

SEQ ID NO:9—Honeybee silk protein termed herein Xenosin (also termed herein AmelSA1) (minus signal peptide).

SEQ ID NO:10—Honeybee silk protein termed herein Xenosin.

SEQ ID NO:11—Nucleotide sequence encoding honeybee silk protein Xenospira1 (minus region encoding signal peptide).

SEQ ID NO:12—Nucleotide sequence encoding honeybee silk protein Xenospira1.

SEQ ID NO:13—Nucleotide sequence encoding honeybee silk protein Xenospira2 (minus region encoding signal peptide).

SEQ ID NO: 14—Nucleotide sequence encoding honeybee silk protein Xenospira2.

SEQ ID NO:15—Nucleotide sequence encoding honeybee silk protein Xenospira3 (minus region encoding signal peptide).

SEQ ID NO:16—Nucleotide sequence encoding honeybee silk protein Xenospira3.

SEQ ID NO:17—Nucleotide sequence encoding honeybee silk protein Xenospira4 (minus region encoding signal peptide).

SEQ ID NO: 18—Nucleotide sequence encoding honeybee silk protein Xenospira4.

SEQ ID NO:19—Nucleotide sequence encoding honeybee silk protein Xenosin (minus region encoding signal peptide). SEQ ID NO:20—Nucleotide sequence encoding honeybee silk protein Xenosin.

SEQ ID NO:21—Gene sequence encoding honeybee silk protein Xenosin.

SEQ ID NO:22—Bumblebee silk protein termed herein BBF1 (minus signal peptide).

SEQ ID NO:23—Bumblebee silk protein termed herein BBF1.

SEQ ID NO:24—Bumblebee silk protein termed herein BBF2 (minus signal peptide).

SEQ ID NO:25—Bumblebee silk protein termed herein BBF2.

SEQ ID NO:26—Bumblebee silk protein termed herein BBF3 (minus signal peptide).

SEQ ID NO:27—Bumblebee silk protein termed herein BBF3.

SEQ ID NO:28—Bumblebee silk protein termed herein BBF4 (minus signal peptide).

SEQ ID NO:29—Bumblebee silk protein termed herein BBF4.

SEQ ID NO:30—Partial amino acid sequence of bumblebee silk protein termed herein BBSA1.

SEQ ID NO:31—Nucleotide sequence encoding bumblebee silk protein BBF1 (minus region encoding signal peptide). SEQ ID NO:32—Nucleotide sequence encoding bumblebee silk protein BBF1.

SEQ ID NO:33—Nucleotide sequence encoding bumblebee silk protein BBF2 (minus region encoding signal peptide). SEQ ID NO:34—Nucleotide sequence encoding bumblebee silk protein BBF2.

SEQ ID NO:35—Nucleotide sequence encoding bumblebee silk protein BBF3 (minus region encoding signal peptide). SEQ ID NO:36—Nucleotide sequence encoding bumblebee silk protein BBF3.

SEQ ID NO:37—Nucleotide sequence encoding bumblebee silk protein BBF4 (minus region encoding signal peptide). SEQ ID NO:38—Nucleotide sequence encoding bumblebee silk protein BBF4.

SEQ ID NO:39—Partial nucleotide sequence encoding bumblebee silk protein BBSA1.

SEQ ID NO:40—Bulldog ant silk protein termed herein BAF1 (minus signal peptide).

SEQ ID NO:41—Bulldog ant silk protein termed herein BAF1.

SEQ ID NO:42—Bulldog ant silk protein termed herein BAF2 (minus signal peptide).

SEQ ID NO:43—Bulldog ant silk protein termed herein BAF2.

SEQ ID NO:44—Bulldog ant silk protein termed herein BAF3 (minus signal peptide).

SEQ ID NO:45—Bulldog ant silk protein termed herein BAF3.

SEQ ID NO:46—Bulldog ant silk protein termed herein BAF4 (minus signal peptide).

SEQ ID NO:47—Bulldog ant silk protein termed herein BAF4.

SEQ ID NO:48—Nucleotide sequence encoding bulldog ant silk protein BAF1 (minus region encoding signal peptide). SEQ ID NO:49—Nucleotide sequence encoding bulldog ant silk protein BAF1.

SEQ ID NO:50—Nucleotide sequence encoding bulldog ant silk protein BAF2 (minus region encoding signal peptide). SEQ ID NO:51—Nucleotide sequence encoding bulldog ant silk protein BAF2.

SEQ ID NO:52—Nucleotide sequence encoding bulldog ant silk protein BAF3 (minus region encoding signal peptide). SEQ ID NO:53—Nucleotide sequence encoding bulldog ant silk protein BAF3.

SEQ ID NO:54—Nucleotide sequence encoding bulldog ant silk protein BAF4 (minus region encoding signal peptide). SEQ ID NO:55—Nucleotide sequence encoding bulldog ant silk protein BAF4.

SEQ ID NO:56—Weaver ant silk protein termed herein GAF1 (minus signal peptide).

SEQ ID NO:57—Weaver ant silk protein termed herein GAF1.

SEQ ID NO:58—Weaver ant silk protein termed herein GAF2 (minus signal peptide).

SEQ ID NO:59—Weaver ant silk protein termed herein GAF2.

SEQ ID NO:60—Weaver ant silk protein termed herein GAF3 (minus signal peptide).

SEQ ID NO:61—Weaver ant silk protein termed herein GAF3.

SEQ ID NO:62—Weaver ant silk protein termed herein GAF4 (minus signal peptide).

SEQ ID NO:63—Weaver ant silk protein termed herein GAF4.

SEQ ID NO:64—Nucleotide sequence encoding weaver ant silk protein GAF1 (minus region encoding signal peptide). SEQ ID NO:65—Nucleotide sequence encoding weaver ant silk protein GAF1.

SEQ ID NO:66—Nucleotide sequence encoding weaver ant silk protein GAF2 (minus region encoding signal peptide). SEQ ID NO:67—Nucleotide sequence encoding weaver ant silk protein GAF2.

SEQ ID NO:68—Nucleotide sequence encoding weaver ant silk protein GAF3 (minus region encoding signal peptide). SEQ ID NO:69—Nucleotide sequence encoding weaver ant silk protein GAF3.

SEQ ID NO:70—Nucleotide sequence encoding weaver ant silk protein GAF4 (minus region encoding signal peptide). SEQ ID NO:71—Nucleotide sequence encoding weaver ant silk protein GAF4.

SEQ ID NO:72—Lacewing silk protein termed herein MalF1 (minus signal peptide).

SEQ ID NO:73—Lacewing silk protein termed herein MalF1.

SEQ ID NO:74—Nucleotide sequence encoding lacewing silk protein MalF1 (minus region encoding signal peptide).

SEQ ID NO:75—Nucleotide sequence encoding lacewing silk protein MalF1.

SEQ ID NO:76—Nucleotide sequence encoding honeybee silk protein termed herein Xenospira4 codon-optimized for plant expression (before subcloning into pET14b and pVEC8).

SEQ ID NO:77—Honeybee silk protein (Xenospira4) open reading frame optimized for plant expression (without translational fusion).

# DETAILED DESCRIPTION OF THE INVENTION

# General Techniques and Definitions

[0135] Unless specifically defined otherwise, all technical and scientific terms used herein shall be taken to have the same meaning as commonly understood by one of ordinary skill in the art (e.g., in cell culture, molecular genetics, immunology, immunohistochemistry, protein chemistry, and biochemistry).

[0136] Unless otherwise indicated, the recombinant protein, cell culture, and immunological techniques utilized in the present invention are standard procedures, well known to those skilled in the art. Such techniques are described and explained throughout the literature in sources such as, J. Perbal, A Practical Guide to Molecular Cloning, John Wiley and Sons (1984), J. Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbour Laboratory Press (1989), T. A. Brown (editor), Essential Molecular Biology: A Practical Approach, Volumes 1 and 2, IRL Press (1991), D. M. Glover and B. D. Hames (editors), DNA Cloning: A Practical Approach, Volumes 1-4, IRL Press (1995 and 1996), and F. M. Ausubel et al. (editors), Current Protocols in Molecular Biology, Greene Pub. Associates and Wiley-Interscience (1988, including all updates until present), Ed Harlow and David Lane (editors) Antibodies: A Laboratory Manual, Cold Spring Harbour Laboratory, (1988), and J. E. Coligan et al. (editors) Current Protocols in Immunology, John Wiley & Sons (including all updates until present), and are incorporated herein by reference.

[0137] As used herein, the terms "silk protein" and "silk polypeptide" refer to a fibrous protein/polypeptide that can be used to produce a silk fibre, and/or a fibrous protein complex. Naturally occurring silk proteins of the invention form part of the brood comb silk of insects such as honeybees, however, as described herein variants of these proteins could readily be produced which would perform the same function if expressed within an appropriate insect.

[0138] As used herein, a "silk fibre" refers to filaments comprising proteins of the invention which can be woven into various items such as textiles.

[0139] As used herein, a "copolymer" is composition comprising two or more silk proteins of the invention. This term excludes naturally occurring copolymers such as the brood comb of insects.

[0140] The term "plant" includes whole plants, vegetative structures (for example, leaves, stems), roots, floral organs/structures, seed (including embryo, endosperm, and seed coat), plant tissue (for example, vascular tissue, ground tissue, and the like), cells and progeny of the same.

[0141] A "transgenic plant" refers to a plant that contains a gene construct ("transgene") not found in a wild-type plant of the same species, variety or cultivar. A "transgene" as referred to herein has the normal meaning in the art of

biotechnology and includes a genetic sequence which has been produced or altered by recombinant DNA or RNA technology and which has been introduced into the plant cell. The transgene may include genetic sequences derived from a plant cell. Typically, the transgene has been introduced into the plant by human manipulation such as, for example, by transformation but any method can be used as one of skill in the art recognizes.

**[0142]** "Polynucleotide" refers to an oligonucleotide, nucleic acid molecule or any fragment thereof. It may be DNA or RNA of genomic or synthetic origin, double-stranded or single-stranded, and combined with carbohydrate, lipids, protein, or other materials to perform a particular activity defined herein.

[0143] "Operably linked" as used herein refers to a functional relationship between two or more nucleic acid (e.g., DNA) segments. Typically, it refers to the functional relationship of transcriptional regulatory element to a transcribed sequence. For example, a promoter is operably linked to a coding sequence, such as a polynucleotide defined herein, if it stimulates or modulates the transcription of the coding sequence in an appropriate host cell. Generally, promoter transcriptional regulatory elements that are operably linked to a transcribed sequence are physically contiguous to the transcribed sequence, i.e., they are cis-acting. However, some transcriptional regulatory elements, such as enhancers, need not be physically contiguous or located in close proximity to the coding sequences whose transcription they enhance.

**[0144]** The term "signal peptide" refers to an amino terminal polypeptide preceding a secreted mature protein. The signal peptide is cleaved from and is therefore not present in the mature protein. Signal peptides have the function of directing and trans-locating secreted proteins across cell membranes. The signal peptide is also referred to as signal sequence.

[0145] As used herein, "transformation" is the acquisition of new genes in a cell by the incorporation of a polynucle-otide

[0146] As used herein, the term "drug" refers to any compound that can be used to treat or prevent a particular disease, examples of drugs which can be formulated with a silk protein of the invention include, but are not limited to, proteins, nucleic acids, anti-tumor agents, analgesics, antibiotics, anti-inflammatory compounds (both steroidal and non-steroidal), hormones, vaccines, labeled substances, and the like.

#### Polypeptides

[0147] By "substantially purified polypeptide" we mean a polypeptide that has generally been separated from the lipids, nucleic acids, other polypeptides, and other contaminating molecules such as wax with which it is associated in its native state. With the exception of other proteins of the invention, it is preferred that the substantially purified polypeptide is at least 60% free, more preferably at least 75% free, and more preferably at least 90% free from other components with which it is naturally associated.

[0148] The term "recombinant" in the context of a polypeptide refers to the polypeptide when produced by a cell, or in a cell-free expression system, in an altered amount or at an altered rate compared to its native state. In one embodiment the cell is a cell that does not naturally produce the polypeptide. However, the cell may be a cell which com-

prises a non-endogenous gene that causes an altered, preferably increased, amount of the polypeptide to be produced. A recombinant polypeptide of the invention includes polypeptides which have not been separated from other components of the transgenic (recombinant) cell, or cell-free expression system, in which it is produced, and polypeptides produced in such cells or cell-free systems which are subsequently purified away from at least some other components

[0149] The terms "polypeptide" and "protein" are generally used interchangeably and refer to a single polypeptide chain which may or may not be modified by addition of non-amino acid groups. The terms "proteins" and "polypeptides" as used herein also include variants, mutants, modifications, analogous and/or derivatives of the polypeptides of the invention as described herein.

[0150] The % identity of a polypeptide is determined by GAP (Needleman and Wunsch, 1970) analysis (GCG program) with a gap creation penalty=5, and a gap extension penalty=0.3. The query sequence is at least 15 amino acids in length, and the GAP analysis aligns the two sequences over a region of at least 15 amino acids. More preferably, the query sequence is at least 50 amino acids in length, and the GAP analysis aligns the two sequences over a region of at least 50 amino acids. More preferably, the query sequence is at least 100 amino acids in length and the GAP analysis aligns the two sequences over a region of at least 100 amino acids. Even more preferably, the query sequence is at least 250 amino acids in length and the GAP analysis aligns the two sequences over a region of at least 250 amino acids. Even more preferably, the GAP analysis aligns the two sequences over their entire length.

[0151] As used herein a "biologically active" fragment is a portion of a polypeptide of the invention which maintains a defined activity of the full-length polypeptide, namely the ability to be used to produce silk. Biologically active fragments can be any size as long as they maintain the defined activity.

[0152] With regard to a defined polypeptide, it will be appreciated that % identity figures higher than those provided above will encompass preferred embodiments. Thus, where applicable, in light of the minimum % identity figures, it is preferred that the polypeptide comprises an amino acid sequence which is at least 40%, more preferably at least 45%, more preferably at least 50%, more preferably at least 55%, more preferably at least 60%, more preferably at least 65%, more preferably at least 70%, more preferably at least 75%, more preferably at least 80%, more preferably at least 85%, more preferably at least 90%, more preferably at least 91%, more preferably at least 92%, more preferably at least 93%, more preferably at least 94%, more preferably at least 95%, more preferably at least 96%, more preferably at least 97%, more preferably at least 98%, more preferably at least 99%, more preferably at least 99.1%, more preferably at least 99.2%, more preferably at least 99.3%, more preferably at least 99.4%, more preferably at least 99.5%, more preferably at least 99.6%, more preferably at least 99.7%, more preferably at least 99.8%, and even more preferably at least 99.9% identical to the relevant nominated SEQ ID NO.

[0153] Amino acid sequence mutants of the polypeptides of the present invention can be prepared by introducing appropriate nucleotide changes into a nucleic acid of the present invention, or by in vitro synthesis of the desired

polypeptide. Such mutants include, for example, deletions, insertions or substitutions of residues within the amino acid sequence. A combination of deletion, insertion and substitution can be made to arrive at the final construct, provided that the final polypeptide product possesses the desired characteristics.

[0154] Mutant (altered) polypeptides can be prepared using any technique known in the art. For example, a polynucleotide of the invention can be subjected to in vitro mutagenesis. Such in vitro mutagenesis techniques include sub-cloning the polynucleotide into a suitable vector, transforming the vector into a "mutator" strain such as the E. coli XL-1 red (Stratagene) and propagating the transformed bacteria for a suitable number of generations. In another example, the polynucleotides of the invention are subjected to DNA shuffling techniques as broadly described by Harayama (1998). These DNA shuffling techniques may include genes of the invention possibly in addition to genes related to those of the present invention, such as silk genes from Hymenopteran or Neuropteran species other than the specific species characterized herein. Products derived from mutated/altered DNA can readily be screened using techniques described herein to determine if they can be used as silk proteins.

[0155] In designing amino acid sequence mutants, the location of the mutation site and the nature of the mutation will depend on characteristic(s) to be modified. The sites for mutation can be modified individually or in series, e.g., by (1) substituting first with conservative amino acid choices and then with more radical selections depending upon the results achieved, (2) deleting the target residue, or (3) inserting other residues adjacent to the located site.

**[0156]** Amino acid sequence deletions generally range from about 1 to 15 residues, more preferably about 1 to 10 residues and typically about 1 to 5 contiguous residues.

[0157] Substitution mutants have at least one amino acid residue in the polypeptide molecule removed and a different residue inserted in its place. The sites of greatest interest for substitutional mutagenesis include sites identified as important for function. Other sites of interest are those in which particular residues obtained from various strains or species are identical. These positions may be important for biological activity. These sites, especially those falling within a sequence of at least three other identically conserved sites, are preferably substituted in a relatively conservative manner. Such conservative substitutions are shown in Table 1 under the heading of "exemplary substitutions".

[0158] As outlined above, a portion of some of the polypeptides of the invention have a coiled coil structure. Coiled coil structures of polypeptides are characterized by heptad repeats represented by the consensus sequence (abcdefg),. In a preferred embodiment, the portion of the polypeptide that has a coiled coil structure comprises at least 10 copies of the heptad sequence abcdefg, and at least 25% of the amino acids at positions a and d are alanine residues.

TABLE 1

Exemplary substitutions	
Original	Exemplary
Residue	Substitutions
Ala (A)	val; leu; ile; gly; cys; ser; thr
Arg (R)	lys

TABLE 1-continued

Exemplary substitutions	
Original Residue	Exemplary Substitutions
Asn (N) Asp (D) Cys (C) Gln (Q) Glu (E) Gly (G) His (H) Ile (I) Leu (L) Lys (K) Met (M) Phe (F) Pro (P) Ser (S) Thr (T) Trp (W) Tyr (Y) Val (V)	gln; his glu Ser; thr; ala; gly; val asn; his asp pro; ala; ser; val; thr asn; gln leu; val; ala; met ile; val; met; ala; phe arg leu; phe leu; val; ala gly thr; ala; gly; val; gln ser; gln; ala tyr trp; phe ile; leu; met; phe; ala; ser; thr

[0159] In a preferred embodiment, the polypeptide that has a coiled coil structure comprises at least 12 consecutive copies, more preferably at least 15 consecutive copies, and even more preferably at least 18 consecutive copies of the heptad. In further embodiments, the polypeptide that has a coiled coil structure can have up to at least 28 copies of the heptad. Typically, the copies of the heptad will be tandemly repeated. However, they do not necessarily have to be perfect tandem repeats, for example, as shown in FIGS. 5 and 6 a few amino acids may be found between two heptads, or a few truncated heptads may be found (see, for example, Xenospira1 in FIG. 5).

[0160] Guidance regarding amino acid substitutions which can be made to the polypeptides of the invention which have a coiled coil structure is provided in FIGS. 5 and 6, as well as Tables 6 to 10. Where a predicted useful amino acid substitution based on the experimental data provided herein is in anyway in conflict with the exemplary substitutions provided in Table 1 it is preferred that a substitution based on the experimental data is used.

[0161] Coiled coil structures of polypeptides of the invention have a high content of alanine residues, particularly at amino acid positions a, d and e of the heptad. However, positions b, c, f and g also have a high frequency of alanine residues. In a preferred embodiment, at least 15% of the amino acids at positions a, d and/or e of the heptads are alanine residues, more preferably at least 25%, more preferably at least 30%, more preferably at least 40%, and even more preferably at least 50%. In a further preferred embodiment, at least 25% of the amino acids at both positions a and d of the heptads are alanine residues, more preferably at least 30%, more preferably at least 40%, and even more preferably at least 50%. Furthermore, it is preferred that at least 15% of the amino acids at positions b, c, f and g of the heptads are alanine residues, more preferably at least 20%, and even more preferably at least 25%.

[0162] Typically, the heptads will not comprise any proline or histidine residues. Furthermore, the heptads will comprise few (1 or 2), if any, phenylalanine, methionine, tyrosine, cysteine, glycine or tryptophan residues. Apart from alanine, common (for example greater than 5%, more preferably greater than 10%) amino acids in the heptads

include leucine (particularly at positions b and d), serine (particularly at positions b, e and f), glutamic acid (particularly at positions c, e and d), lysine (particularly at positions b, c, d, f and g) as well as arginine at position g.

[0163] Polypeptides (and polynucleotides) of the invention can be purified (isolated) from a wide variety of Hymenopteran and Neuropteran species. Examples of Hymenopterans include, but are not limited to, any species of the Suborder Apocrita (bees, ants and wasps), which include the following Families of insects; Chrysididae (cuckoo wasps), Formicidae (ants), Mutillidae (velvet ants), Pompilidae (spider wasps), Scoliidae, Vespidae (paper wasps, potter wasps, hornets), Agaonidae (fig wasps), Chalcididae (chalcidids), Eucharitidae (eucharitids), Eupelmidae (eupelmids), Pteromalidae (pteromalids), Evaniidae (ensign wasps), Braconidae, Ichneumonidae (ichneumons), Megachilidae, Apidae, Colletidae, Halictidae, and Melittidae (oil collecting bees). Examples of Neuropterans include species from the following insect Families: Mantispidae, Chrysopidae (lacewings), Myrmeleontidae (antlions), and Ascalaphidae (owlflies). Such further polypeptides (and polynucleotides) can be characterized using the same procedures described herein for silks from Bombus terrestris, Myrmecia forficata, Oecophylla smaragdina and Mallada signata.

[0164] Furthermore, if desired, unnatural amino acids or chemical amino acid analogues can be introduced as a substitution or addition into the polypeptides of the present invention. Such amino acids include, but are not limited to, the D-isomers of the common amino acids, 2,4-diaminobutyric acid,  $\alpha$ -amino isobutyric acid, 4-aminobutyric acid, 2-amino butyric acid, 6-amino hexanoic acid, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-butylglanine, phenylglycine, cyclohexylalanine,  $\beta$ -alanine, fluoro-amino acids, designer amino acids such as  $\beta$ -methyl amino acids,  $\alpha$ -methyl amino acids, and amino acid analogues in general.

[0165] Also included within the scope of the invention are polypeptides of the present invention which are differentially modified during or after synthesis, e.g., by biotinylation, benzylation, glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. These modifications may serve to increase the stability and/or bioactivity of the polypeptide of the invention.

[0166] Polypeptides of the present invention can be produced in a variety of ways, including production and recovery of natural polypeptides, production and recovery of recombinant polypeptides, and chemical synthesis of the polypeptides. In one embodiment, an isolated polypeptide of the present invention is produced by culturing a cell capable of expressing the polypeptide under conditions effective to produce the polypeptide, and recovering the polypeptide. A preferred cell to culture is a recombinant cell of the present invention. Effective culture conditions include, but are not limited to, effective media, bioreactor, temperature, pH and oxygen conditions that permit polypeptide production. An effective medium refers to any medium in which a cell is cultured to produce a polypeptide of the present invention. Such medium typically comprises an aqueous medium having assimilable carbon, nitrogen and phosphate sources, and appropriate salts, minerals, metals and other nutrients, such as vitamins. Cells of the present invention can be cultured in conventional fermentation bioreactors, shake flasks, test tubes, microtiter dishes, and petri plates. Culturing can be carried out at a temperature, pH and oxygen content appropriate for a recombinant cell. Such culturing conditions are within the expertise of one of ordinary skill in the art.

[0167] Polynucleotides

[0168] By an "isolated polynucleotide", including DNA, RNA, or a combination of these, single or double stranded, in the sense or antisense orientation or a combination of both, dsRNA or otherwise, we mean a polynucleotide which is at least partially separated from the polynucleotide sequences with which it is associated or linked in its native state. Preferably, the isolated polynucleotide is at least 60% free, preferably at least 75% free, and most preferably at least 90% free from other components with which they are naturally associated. Furthermore, the term "polynucleotide" is used interchangeably herein with the term "nucleic acid".

[0169] The term "exogenous" in the context of a polynucleotide refers to the polynucleotide when present in a cell, or in a cell-free expression system, in an altered amount compared to its native state. In one embodiment, the cell is a cell that does not naturally comprise the polynucleotide. However, the cell may be a cell which comprises a nonendogenous polynucleotide resulting in an altered, preferably increased, amount of production of the encoded polypeptide. An exogenous polynucleotide of the invention includes polynucleotides which have not been separated from other components of the transgenic (recombinant) cell, or cell-free expression system, in which it is present, and polynucleotides produced in such cells or cell-free systems which are subsequently purified away from at least some other components.

[0170] The % identity of a polynucleotide is determined by GAP (Needleman and Wunsch, 1970) analysis (GCG program) with a gap creation penalty=5, and a gap extension penalty=0.3. Unless stated otherwise, the query sequence is at least 45 nucleotides in length, and the GAP analysis aligns the two sequences over a region of at least 45 nucleotides. Preferably, the query sequence is at least 150 nucleotides in length, and the GAP analysis aligns the two sequences over a region of at least 150 nucleotides. More preferably, the query sequence is at least 300 nucleotides in length and the GAP analysis aligns the two sequences over a region of at least 300 nucleotides. Even more preferably, the GAP analysis aligns the two sequences over their entire length.

[0171] With regard to the defined polynucleotides, it will be appreciated that % identity figures higher than those provided above will encompass preferred embodiments. Thus, where applicable, in light of the minimum % identity figures, it is preferred that a polynucleotide of the invention comprises a sequence which is at least 40%, more preferably at least 45%, more preferably at least 50%, more preferably at least 55%, more preferably at least 60%, more preferably at least 65%, more preferably at least 70%, more preferably at least 75%, more preferably at least 80%, more preferably at least 85%, more preferably at least 90%, more preferably at least 91%, more preferably at least 92%, more preferably at least 93%, more preferably at least 94%, more preferably at least 95%, more preferably at least 96%, more preferably at least 97%, more preferably at least 98%, more preferably at least 99%, more preferably at least 99.1%, more preferably at least 99.2%, more preferably at least 99.3%, more preferably at least 99.4%, more preferably at least 99.5%, more preferably at least 99.6%, more preferably at least 99.7%, more preferably at least 99.8%, and even more preferably at least 99.9% identical to the relevant nominated SEQ ID NO.

[0172] Polynucleotides of the present invention may possess, when compared to naturally occurring molecules, one or more mutations which are deletions, insertions, or substitutions of nucleotide residues. Mutants can be either naturally occurring (that is to say, isolated from a natural source) or synthetic (for example, by performing site-directed mutagenesis on the nucleic acid).

[0173] Oligonucleotides and/or polynucleotides of the invention hybridize to a silk gene of the present invention, or a region flanking said gene, under stringent conditions. The term "stringent hybridization conditions" and the like as used herein refers to parameters with which the art is familiar, including the variation of the hybridization temperature with length of an oligonucleotide. Nucleic acid hybridization parameters may be found in references which compile such methods, Sambrook, et al. (supra), and Ausubel, et al. (supra). For example, stringent hybridization conditions, as used herein, can refer to hybridization at 65° C. in hybridization buffer (3.5×SSC, 0.02%. Ficoll, 0.02% polyvinyl pyrrolidone, 0.02% Bovine Serum Albumin (BSA), 2.5 mM NaH<sub>2</sub>PO<sub>4</sub> (pH7), 0.5% SDS, 2 mM EDTA), followed by one or more washes in 0.2×SSC, 0.01% BSA at 50° C. Alternatively, the nucleic acid and/or oligonucleotides (which may also be referred to as "primers" or "probes") hybridize to the region of the an insect genome of interest, such as the genome of a honeybee, under conditions used in nucleic acid amplification techniques such as PCR. [0174] Oligonucleotides of the present invention can be RNA, DNA, or derivatives of either. Although the terms polynucleotide and oligonucleotide have overlapping meaning, oligonucleotides are typically relatively short single stranded molecules. The minimum size of such oligonucleotides is the size required for the formation of a stable hybrid between an oligonucleotide and a complementary sequence on a target nucleic acid molecule. Preferably, the oligonucleotides are at least 15 nucleotides, more preferably at least 18 nucleotides, more preferably at least 19 nucleotides, more preferably at least 20 nucleotides, even more preferably at least 25 nucleotides in length.

[0175] Usually, monomers of a polynucleotide or oligonucleotide are linked by phosphodiester bonds or analogs thereof to form oligonucleotides ranging in size from a relatively short monomeric units, e.g., 12-18, to several hundreds of monomeric units. Analogs of phosphodiester linkages include: phosphorothioate, phosphoroatilioate, phosphoroanilothioate, phosphoranilidate, phosphoramidate.

[0176] The present invention includes oligonucleotides that can be used as, for example, probes to identify nucleic acid molecules, or primers to produce nucleic acid molecules. Oligonucleotides of the present invention used as a probe are typically conjugated with a detectable label such as a radioisotope, an enzyme, biotin, a fluorescent molecule or a chemiluminescent molecule.

# Recombinant Vectors

[0177] One embodiment of the present invention includes a recombinant vector, which comprises at least one isolated polynucleotide molecule of the present invention, inserted

into any vector capable of delivering the polynucleotide molecule into a host cell. Such a vector contains heterologous polynucleotide sequences, that is polynucleotide sequences that are not naturally found adjacent to polynucleotide molecules of the present invention and that preferably are derived from a species other than the species from which the polynucleotide molecule(s) are derived. The vector can be either RNA or DNA, either prokaryotic or eukaryotic, and typically is a transposon (such as described in U.S. Pat. No. 5,792,294), a virus or a plasmid.

[0178] One type of recombinant vector comprises a polynucleotide molecule of the present invention operatively linked to an expression vector. The phrase operatively linked refers to insertion of a polynucleotide molecule into an expression vector in a manner such that the molecule is able to be expressed when transformed into a host cell. As used herein, an expression vector is a DNA or RNA vector that is capable of transforming a host cell and of effecting expression of a specified polynucleotide molecule. Preferably, the expression vector is also capable of replicating within the host cell. Expression vectors can be either prokaryotic or eukaryotic, and are typically viruses or plasmids. Expression vectors of the present invention include any vectors that function (i.e., direct gene expression) in recombinant cells of the present invention, including in bacterial, fungal, endoparasite, arthropod, animal, and plant cells. Particularly preferred expression vectors of the present invention can direct gene expression in plants cells. Vectors of the invention can also be used to produce the polypeptide in a cell-free expression system, such systems are well known in the art.

[0179] In particular, expression vectors of the present invention contain regulatory sequences such as transcription control sequences, translation control sequences, origins of replication, and other regulatory sequences that are compatible with the recombinant cell and that control the expression of polynucleotide molecules of the present invention. In particular, recombinant molecules of the present invention include transcription control sequences. Transcription control sequences are sequences which control the initiation, elongation, and termination of transcription. Particularly important transcription control sequences are those which control transcription initiation, such as promoter, enhancer, operator and repressor sequences. Suitable transcription control sequences include any transcription control sequence that can function in at least one of the recombinant cells of the present invention. A variety of such transcription control sequences are known to those skilled in the art. Preferred transcription control sequences include those which function in bacterial, yeast, arthropod, plant or mammalian cells, such as, but not limited to, tac, lac, trp, trc, oxy-pro, omp/lpp, rrnB, bacteriophage lambda, bacteriophage T7, T7lac, bacteriophage T3, bacteriophage SP6, bacteriophage SP01, metallothionein, alpha-mating factor, Pichia alcohol oxidase, alphavirus subgenomic promoters (such as Sindbis virus subgenomic promoters), antibiotic resistance gene, baculovirus, Heliothis zea insect virus, vaccinia virus, herpesvirus, raccoon poxvirus, other poxvirus, adenovirus, cytomegalovirus (such as intermediate early promoters), simian virus 40, retrovirus, actin, retroviral long terminal repeat, Rous sarcoma virus, heat shock, phosphate and nitrate transcription control sequences as well as other sequences capable of controlling gene expression in prokaryotic or eukaryotic cells.

[0180] Particularly preferred transcription control sequences are promoters active in directing transcription in plants, either constitutively or stage and/or tissue specific, depending on the use of the plant or parts thereof. These plant promoters include, but are not limited to, promoters showing constitutive expression, such as the 35S promoter of Cauliflower Mosaic Virus (CaMV), those for leaf-specific expression, such as the promoter of the ribulose bisphosphate carboxylase small subunit gene, those for root-specific expression, such as the promoter from the glutamine synthase gene, those for seed-specific expression, such as the cruciferin A promoter from *Brassica napus*, those for tuber-specific expression, such as the class-I patatin promoter from potato or those for fruit-specific expression, such as the polygalacturonase (PG) promoter from tomato.

[0181] Recombinant molecules of the present invention may also (a) contain secretory signals (i.e., signal segment nucleic acid sequences) to enable an expressed polypeptide of the present invention to be secreted from the cell that produces the polypeptide and/or (b) contain fusion sequences which lead to the expression of nucleic acid molecules of the present invention as fusion proteins. Examples of suitable signal segments include any signal segment capable of directing the secretion of a polypeptide of the present invention. Preferred signal segments include, but are not limited to, tissue plasminogen activator (t-PA), interferon, interleukin, growth hormone, viral envelope glycoprotein signal segments, Nicotiana nectarin signal peptide (U.S. Pat. No. 5,939,288), tobacco extensin signal, the soy oleosin oil body binding protein signal, Arabidopsis thaliana vacuolar basic chitinase signal peptide, as well as native signal sequences of a polypeptide of the invention. In addition, a nucleic acid molecule of the present invention can be joined to a fusion segment that directs the encoded polypeptide to the proteosome, such as a ubiquitin fusion segment. Recombinant molecules may also include intervening and/or untranslated sequences surrounding and/or within the nucleic acid sequences of the present invention.

# Host Cells

[0182] Another embodiment of the present invention includes a recombinant cell comprising a host cell transformed with one or more recombinant molecules of the present invention, or progeny cells thereof. Transformation of a polynucleotide molecule into a cell can be accomplished by any method by which a polynucleotide molecule can be inserted into the cell. Transformation techniques include, but are not limited to, transfection, electroporation, microinjection, lipofection, adsorption, and protoplast fusion. A recombinant cell may remain unicellular or may grow into a tissue, organ or a multicellular organism. Transformed polynucleotide molecules of the present invention can remain extrachromosomal or can integrate into one or more sites within a chromosome of the transformed (i.e., recombinant) cell in such a manner that their ability to be expressed is retained. [0183] Suitable host cells to transform include any cell that can be transformed with a polynucleotide of the present invention. Host cells of the present invention either can be endogenously (i.e., naturally) capable of producing polypeptides of the present invention or can be capable of producing such polypeptides after being transformed with at least one polynucleotide molecule of the present invention. Host cells of the present invention can be any cell capable of producing at least one protein of the present invention,

and include bacterial, fungal (including yeast), parasite, arthropod, animal and plant cells. Examples of host cells include Salmonella, Escherichia, Bacillus, Listeria, Saccharomyces, Spodoptera, Mycobacterta, Trichoplusia, BHK (baby hamster kidney) cells, MDCK cells, CRFK cells, CV-1 cells, COS (e.g., COS-7) cells, and Vero cells. Further examples of host cells are E. coli, including E. coli K-12 derivatives; Salmonella typhi; Salmonella typhimurium, including attenuated strains; Spodoptera frugiperda; Trichoplusia ni; and non-tumorigenic mouse myoblast G8 cells (e.g., ATCC CRL 1246). Additional appropriate mammalian cell hosts include other kidney cell lines, other fibroblast cell lines (e.g., human, murine or chicken embryo fibroblast cell lines), myeloma cell lines, Chinese hamster ovary cells, mouse NIH/3T3 cells, LMTK cells and/or HeLa cells. Particularly preferred host cells are plant cells such as those available from Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (German Collection of Microorganisms and Cell Cultures).

[0184] Recombinant DNA technologies can be used to improve expression of a transformed polynucleotide molecule by manipulating, for example, the number of copies of the polynucleotide molecule within a host cell, the efficiency with which those polynucleotide molecules are transcribed, the efficiency with which the resultant transcripts are translated, and the efficiency of post-translational modifications. Recombinant techniques useful for increasing the expression of polynucleotide molecules of the present invention include, but are not limited to, operatively linking polynucleotide molecules to high-copy number plasmids, integration of the polynucleotide molecule into one or more host cell chromosomes, addition of vector stability sequences to plasmids, substitutions or modifications of transcription control signals (e.g., promoters, operators, enhancers), substitutions or modifications of translational control signals (e.g., ribosome binding sites, Shine-Dalgarno sequences), modification of polynucleotide molecules of the present invention to correspond to the codon usage of the host cell, and the deletion of sequences that destabilize transcripts.

# Transgenic Plants

[0185] The term "plant" refers to whole plants, plant organs (e.g. leaves, stems roots, etc), seeds, plant cells and the like. Plants contemplated for use in the practice of the present invention include both monocotyledons and dicotyledons. Target plants include, but are not limited to, the following: cereals (wheat, barley, rye, oats, rice, sorghum and related crops); beet (sugar beet and fodder beet); pomes, stone fruit and soft fruit (apples, pears, plums, peaches, almonds, cherries, strawberries, raspberries and black-berries); leguminous plants (beans, lentils, peas, soybeans); oil plants (rape, mustard, poppy, olives, sunflowers, coconut, castor oil plants, cocoa beans, groundnuts); cucumber plants (marrows, cucumbers, melons); fibre plants (cotton, flax, hemp, jute); citrus fruit (oranges, lemons, grapefruit, mandarins); vegetables (spinach, lettuce, asparagus, cabbages, carrots, onions, tomatoes, potatoes, paprika); lauraceae (avocados, cinnamon, camphor); or plants such as maize, tobacco, nuts, coffee, sugar cane, tea, vines, hops, turf, bananas and natural rubber plants, as well as ornamentals (flowers, shrubs, broad-leaved trees and evergreens, such as conifers).

[0186] Transgenic plants, as defined in the context of the present invention include plants (as well as parts and cells of

said plants) and their progeny which have been genetically modified using recombinant techniques to cause production of at least one polypeptide of the present invention in the desired plant or plant organ. Transgenic plants can be produced using techniques known in the art, such as those generally described in A. Slater et al., Plant Biotechnology—The Genetic Manipulation of Plants, Oxford University Press (2003), and P. Christou and H. Klee, Handbook of Plant Biotechnology, John Wiley and Sons (2004).

[0187] A polynucleotide of the present invention may be expressed constitutively in the transgenic plants during all stages of development. Depending on the use of the plant or plant organs, the polypeptides may be expressed in a stage-specific manner. Furthermore, the polynucleotides may be expressed tissue-specifically.

[0188] Regulatory sequences which are known or are found to cause expression of a gene encoding a polypeptide of interest in plants may be used in the present invention. The choice of the regulatory sequences used depends on the target plant and/or target organ of interest. Such regulatory sequences may be obtained from plants or plant viruses, or may be chemically synthesized. Such regulatory sequences are well known to those skilled in the art.

[0189] Constitutive plant promoters are well known. Further to previously mentioned promoters, some other suitable promoters include but are not limited to the nopaline synthase promoter, the octopine synthase promoter, CaMV 35S promoter, the ribulose-1,5-bisphosphate carboxylase promoter, Adh1-based pEmu, Act1, the SAM synthase promoter and Ubi promoters and the promoter of the chlorophyll a/b binding protein. Alternatively it may be desired to have the transgene(s) expressed in a regulated fashion. Regulated expression of the polypeptides is possible by placing the coding sequence of the silk protein under the control of promoters that are tissue-specific, developmental-specific, or inducible. Several tissue-specific regulated genes and/or promoters have been reported in plants. These include genes encoding the seed storage proteins (such as napin, cruciferin, β-conglycinin, glycinin and phaseolin), zein or oil body proteins (such as oleosin), or genes involved in fatty acid biosynthesis (including acyl carrier protein, stearoyl-ACP desaturase, and fatty acid desaturases (fad 2-1)), and other genes expressed during embryo development (such as Bce4). Particularly useful for seed-specific expression is the pea vicilin promoter. Other useful promoters for expression in mature leaves are those that are switched on at the onset of senescence, such as the SAG promoter from Arabidopsis). A class of fruit-specific promoters expressed at or during anthesis through fruit development, at least until the beginning of ripening, is discussed in U.S. Pat. No. 4,943, 674. Other examples of tissue-specific promoters include those that direct expression in tubers (for example, patatin gene promoter), and in fiber cells (an example of a developmentally-regulated fiber cell protein is E6 fiber).

[0190] Other regulatory sequences such as terminator sequences and polyadenylation signals include any such sequence functioning as such in plants, the choice of which would be obvious to the skilled addressee. The termination region used in the expression cassette will be chosen primarily for convenience, since the termination regions appear to be relatively interchangeable. The termination region which is used may be native with the transcriptional initiation region, may be native with the polynucleotide sequence of interest, or may be derived from another source. The

termination region may be naturally occurring, or wholly or partially synthetic. Convenient termination regions are available from the Ti-plasmid of *A. tumefaciens*, such as the octopine synthase and nopaline synthase termination regions or from the genes for  $\beta$ -phaseolin, the chemically inducible lant gene, plN.

[0191] Several techniques are available for the introduction of an expression construct containing a nucleic acid sequence encoding a polypeptide of interest into the target plants. Such techniques include but are not limited to transformation of protoplasts using the calcium/polyethylene glycol method, electroporation and microinjection or (coated) particle bombardment. In addition to these so-called direct DNA transformation methods, transformation systems involving vectors are widely available, such as viral and bacterial vectors (e.g. from the genus *Agrobacterium*). After selection and/or screening, the protoplasts, cells or plant parts that have been transformed can be regenerated into whole plants, using methods known in the art. The choice of the transformation and/or regeneration techniques is not critical for this invention.

[0192] To confirm the presence of the transgenes in transgenic cells and plants, a polymerase chain reaction (PCR) amplification or Southern blot analysis can be performed using methods known to those skilled in the art. Expression products of the transgenes can be detected in any of a variety of ways, depending upon the nature of the product, and include Western blot and enzyme assay. One particularly useful way to quantitate protein expression and to detect replication in different plant tissues is to use a reporter gene, such as GUS. Once transgenic plants have been obtained, they may be grown to produce plant tissues or parts having the desired phenotype. The plant tissue or plant parts, may be harvested, and/or the seed collected. The seed may serve as a source for growing additional plants with tissues or parts having the desired characteristics.

#### Transgenic Hon-Human Animals

[0193] Techniques for producing transgenic animals are well known in the art. A useful general textbook on this subject is Houdebine, Transgenic animals—Generation and Use (Harwood Academic, 1997).

[0194] Heterologous DNA can be introduced, for example, into fertilized mammalian ova. For instance, totipotent or pluripotent stem cells can be transformed by microinjection, calcium phosphate mediated precipitation, liposome fusion, retroviral infection or other means, the transformed cells are then introduced into the embryo, and the embryo then develops into a transgenic animal. In a highly preferred method, developing embryos are infected with a retrovirus containing the desired DNA, and transgenic animals produced from the infected embryo. In a most preferred method, however, the appropriate DNAs are coinjected into the pronucleus or cytoplasm of embryos, preferably at the single cell stage, and the embryos allowed to develop into mature transgenic animals.

[0195] Another method used to produce a transgenic animal involves microinjecting a nucleic acid into pro-nuclear stage eggs by standard methods. Injected eggs are then cultured before transfer into the oviducts of pseudopregnant recipients.

[0196] Transgenic animals may also be produced by nuclear transfer technology. Using this method, fibroblasts from donor animals are stably transfected with a plasmid

incorporating the coding sequences for a binding domain or binding partner of interest under the control of regulatory sequences. Stable transfectants are then fused to enucleated oocytes, cultured and transferred into female recipients.

Recovery Methods and Production of Silk

[0197] The silk proteins of the present invention may be extracted and purified from recombinant cells, such as plant, bacteria or yeast cells, producing said protein by a variety of methods. In one embodiment, the method involves removal of native cell proteins from homogenized cells/tissues/plants etc. by lowering pH and heating, followed by ammonium sulfate fractionation. Briefly, total soluble proteins are extracted by homogenizing cells/tissues/plants. Native proteins are removed by precipitation at pH 4.7 and then at 60° C. The resulting supernatant is then fractionated with ammonium sulfate at 40% saturation. The resulting protein will be of the order of 95% pure. Additional purification may be achieved with conventional gel or affinity chromatography.

[0198] In another example, cell lysates are treated with high concentrations of acid e.g. HCl or propionic acid to reduce pH to ~1-2 for 1 hour or more which will solubilise the silk proteins but precipitate other proteins.

[0199] Fibrillar aggregates will form from solutions by spontaneous self-assembly of silk proteins of the invention when the protein concentration exceeds a critical value. The aggregates may be gathered and mechanically spun into macroscopic fibers according to the method of O'Brien et al. (I. O'Brien et al., "Design, Synthesis and Fabrication of Novel Self-Assembling Fibrillar Proteins", in Silk Polymers: Materials Science and Biotechnology, pp. 104-117, Kaplan, Adams, Farmer and Viney, eds., c. 1994 by American Chemical Society, Washington, D.C.).

[0200] By nature of the inherent coiled coil secondary structure, proteins such as Xenospira1-4, BBF1-4, BAF1-4 and GAF1-4 will spontaneously form the coiled coil secondary structure upon dehydration. As described below, the strength of the coiled coil can be enhanced through enzymatic or chemical cross-linking of lysine residues in close proximity.

[0201] Silk fibres and/or copolymers of the invention have a low processing requirement. The silk proteins of the invention require minimal processing e.g. spinning to form a strong fibre as they spontaneously forms strong coiled coils which can be reinforced with crosslinks such as lysine crosslinks. This contrasts with  $B.\ mori$  and spider recombinant silk polypeptides which require sophisticated spinning techniques in order to obtain the secondary structure ( $\beta$ -sheet) and strength of the fibre.

[0202] However, fibers may be spun from solutions having properties characteristic of a liquid crystal phase. The fiber concentration at which phase transition can occur is dependent on the composition of a protein or combination of proteins present in the solution. Phase transition, however, can be detected by monitoring the clarity and birefringence of the solution. Onset of a liquid crystal phase can be detected when the solution acquires a translucent appearance and registers birefringence when viewed through crossed polarizing filters.

[0203] In one fiber-forming technique, fibers can first be extruded from the protein solution through an orifice into methanol, until a length sufficient to be picked up by a mechanical means is produced. Then a fiber can be pulled by

such mechanical means through a methanol solution, collected, and dried. Methods for drawing fibers are considered well-known in the art.

[0204] Further examples of methods which may be used for producing silk fibres and/or copolymers of the present are described in US 2004/0170827 and US 2005/0054830. [0205] In a preferred embodiment, silk fibres and/or copolymers of the invention are crosslinked. In one embodiment, the silk fibres and/or copolymers are crosslinked to a surface/article/product etc of interest using techniques known in the art. In another embodiment (or in combination with the previous embodiment), at least some silk proteins in the silk fibres and/or copolymers are crosslinked to each other. Preferably, the silk proteins are crosslinked via lysine residues in the proteins. Such crosslinking can be performed using chemical and/or enzymatic techniques known in the art. For example, enzymatic cross links can be catalysed by lysyl oxidase, whereas nonenzymatic cross links can be generated from glycated lysine residues (Reiser et al., 1992).

#### Antibodies

[0206] The invention also provides monoclonal or polyclonal antibodies to polypeptides of the invention or fragments thereof. Thus, the present invention further provides a process for the production of monoclonal or polyclonal antibodies to polypeptides of the invention.

[0207] The term "binds specifically" refers to the ability of the antibody to bind to at least one polypeptide of the present invention but not other known silk proteins.

[0208] As used herein, the term "epitope" refers to a region of a polypeptide of the invention which is bound by the antibody. An epitope can be administered to an animal to generate antibodies against the epitope, however, antibodies of the present invention preferably specifically bind the epitope region in the context of the entire polypeptide.

[0209] If polyclonal antibodies are desired, a selected mammal (e.g., mouse, rabbit, goat, horse, etc.) is immunised with an immunogenic polypeptide of the invention. Serum from the immunised animal is collected and treated according to known procedures. If serum containing polyclonal antibodies contains antibodies to other antigens, the polyclonal antibodies can be purified by immunoaffinity chromatography. Techniques for producing and processing polyclonal antisera are known in the art. In order that such antibodies may be made, the invention also provides polypeptides of the invention or fragments thereof haptenised to another polypeptide for use as immunogens in animals.

[0210] Monoclonal antibodies directed against polypeptides of the invention can also be readily produced by one skilled in the art. The general methodology for making monoclonal antibodies by hybridomas is well known. Immortal antibody-producing cell lines can be created by cell fusion, and also by other techniques such as direct transformation of B lymphocytes with oncogenic DNA, or transfection with Epstein-Barr virus. Panels of monoclonal antibodies produced can be screened for various properties; i.e., for isotype and epitope affinity.

[0211] An alternative technique involves screening phage display libraries where, for example the phage express scFv fragments on the surface of their coat with a large variety of complementarity determining regions (CDRs). This technique is well known in the art.

[0212] For the purposes of this invention, the term "antibody", unless specified to the contrary, includes fragments of whole antibodies which retain their binding activity for a target antigen. Such fragments include Fv, F(ab') and F(ab')<sub>2</sub> fragments, as well as single chain antibodies (scFv). Furthermore, the antibodies and fragments thereof may be humanised antibodies, for example as described in EP-A-239400

[0213] Antibodies of the invention may be bound to a solid support and/or packaged into kits in a suitable container along with suitable reagents, controls, instructions and the like.

[0214] Preferably, antibodies of the present invention are detectably labeled. Exemplary detectable labels that allow for direct measurement of antibody binding include radiolabels, fluorophores, dyes, magnetic beads, chemiluminescers, colloidal particles, and the like. Examples of labels which permit indirect measurement of binding include enzymes where the substrate may provide for a coloured or fluorescent product. Additional exemplary detectable labels include covalently bound enzymes capable of providing a detectable product signal after addition of suitable substrate. Examples of suitable enzymes for use in conjugates include horseradish peroxidase, alkaline phosphatase, malate dehydrogenase and the like. Where not commercially available, such antibody-enzyme conjugates are readily produced by techniques known to those skilled in the art. Further exemplary detectable labels include biotin, which binds with high affinity to avidin or streptavidin; fluorochromes (e.g., phycobiliproteins, phycoerythrin and allophycocyanins; fluorescein and Texas red), which can be used with a fluorescence activated cell sorter; haptens; and the like. Preferably, the detectable label allows for direct measurement in a plate luminometer, e.g., biotin. Such labeled antibodies can be used in techniques known in the art to detect polypeptides of the invention.

## Compositions

[0215] Compositions of the present invention may include an "acceptable carrier". Examples of such acceptable carriers include water, saline, Ringer's solution, dextrose solution, Hank's solution, and other aqueous physiologically balanced salt solutions. Nonaqueous vehicles, such as fixed oils, sesame oil, ethyl oleate, or triglycerides may also be used.

[0216] In one embodiment, the "acceptable carrier" is a "pharmaceutically acceptable carrier". The term pharmaceutically acceptable carrier refers to molecular entities and compositions that do not produce an allergic, toxic or otherwise adverse reaction when administered to an animal, particularly a mammal, and more particularly a human. Useful examples of pharmaceutically acceptable carriers or diluents include, but are not limited to, solvents, dispersion media, coatings, stabilizers, protective colloids, adhesives, thickeners, thixotropic agents, penetration agents, sequestering agents and isotonic and absorption delaying agents that do not affect the activity of the polypeptides of the invention. The proper fluidity can be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. More generally, the polypeptides of the invention can be combined with any non-toxic solid or liquid additive corresponding to the usual formulating techniques.

[0217] As outlined herein, in some embodiments a polypeptide, a silk fiber and/or a copolymer of the invention is used as a pharmaceutically acceptable carrier.

[0218] Other suitable compositions are described below with specific reference to specific uses of the polypeptides of the invention.

#### Uses

[0219] Silk proteins are useful for the creation of new biomaterials because of their exceptional toughness and strength. However, to date the fibrous proteins of spiders and insects are large proteins (over 100 kDa) and consist of highly repetitive amino acid sequences. These proteins are encoded by large genes containing highly biased codons making them particularly difficult to produce in recombinant systems. By comparison, the silk proteins of the invention are short and non-repetitive. These properties make the genes encoding these proteins particularly attractive for recombinant production of new biomaterials.

[0220] The silk proteins, silk fibers and/or copolymers of the invention can be used for a broad and diverse array of medical, military, industrial and commercial applications. The fibers can be used in the manufacture of medical devices such as sutures, skin grafts, cellular growth matrices, replacement ligaments, and surgical mesh, and in a wide range of industrial and commercial products, such as, for example, cable, rope, netting, fishing line, clothing fabric, bullet-proof vest lining, container fabric, backpacks, knapsacks, bag or purse straps, adhesive binding material, nonadhesive binding material, strapping material, tent fabric, tarpaulins, pool covers, vehicle covers, fencing material, sealant, construction material, weatherproofing material, flexible partition material, sports equipment; and, in fact, in nearly any use of fiber or fabric for which high tensile strength and elasticity are desired characteristics. The silk proteins, silk fibers and/or copolymers of the present invention also have applications in compositions for personal care products such as cosmetics, skin care, hair care and hair colouring; and in coating of particles, such as pigments.

[0221] The silk proteins may be used in their native form or they may be modified to form derivatives, which provide a more beneficial effect. For example, the silk protein may be modified by conjugation to a polymer to reduce allergenicity as described in U.S. Pat. No. 5,981,718 and U.S. Pat. No. 5,856,451. Suitable modifying polymers include, but are not limited to, polyalkylene oxides, polyvinyl alcohol, polycarboxylates, poly(vinylpyrrolidone), and dextrans. In another example, the silk proteins may be modified by selective digestion and splicing of other protein modifiers. For example, the silk proteins may be cleaved into smaller peptide units by treatment with acid at an elevated temperature of about 60° C. The useful acids include, but are not limited to, dilute hydrochloric, sulfuric or phosphoric acids. Alternatively, digestion of the silk proteins may be done by treatment with a base, such as sodium hydroxide, or enzymatic digestion using a suitable protease may be used.

[0222] The proteins may be further modified to provide performance characteristics that are beneficial in specific applications for personal care products. The modification of proteins for use in personal care products is well known in the art. For example, commonly used methods are described in U.S. Pat. No. 6,303,752, U.S. Pat. No. 6,284,246, and U.S. Pat. No. 6,358,501. Examples of modifications include, but are not limited to, ethoxylation to promote water-oil

emulsion enhancement, siloxylation to provide lipophilic compatibility, and esterification to aid in compatibility with soap and detergent compositions. Additionally, the silk proteins may be derivatized with functional groups including, but not limited to, amines, oxiranes, cyanates, carboxylic acid esters, silicone copolyols, siloxane esters, quaternized amine aliphatics, urethanes, polyacrylamides, dicarboxylic acid esters, and halogenated esters. The silk proteins may also be derivatized by reaction with diimines and by the formation of metal salts.

[0223] Consistent with the above definitions of "polypeptide" (and "protein"), such derivatized and/or modified molecules are also referred to herein broadly as "polypeptides" and "proteins".

[0224] Silk proteins of the invention can be spun together and/or bundled or braided with other fiber types. Examples include, but are not limited to, polymeric fibers (e.g., polypropylene, nylon, polyester), fibers and silks of other plant and animal sources (e.g., cotton, wool, *Bombyx mori* or spider silk), and glass fibers. A preferred embodiment is silk fiber braided with 10% polypropylene fiber. The present invention contemplates that the production of such combinations of fibers can be readily practiced to enhance any desired characteristics, e.g., appearance, softness, weight, durability, water-repellant properties, improved cost-of-manufacture, that may be generally sought in the manufacture and production of fibers for medical, industrial, or commercial applications.

# Personal Care Products

[0225] Cosmetic and skin care compositions may be anhydrous compositions comprising an effective amount of silk protein in a cosmetically acceptable medium. The uses of these compositions include, but are not limited to, skin care, skin cleansing, make-up, and anti-wrinkle products. An effective amount of a silk protein for cosmetic and skin care compositions is herein defined as a proportion of from about  $10^{-4}$  to about 30% by weight, but preferably from about  $10^{-3}$ to 15% by weight, relative to the total weight of the composition. This proportion may vary as a function of the type of cosmetic or skin care composition. Suitable compositions for a cosmetically acceptable medium are described in U.S. Pat. No. 6,280,747. For example, the cosmetically acceptable medium may contain a fatty substance in a proportion generally of from about 10 to about 90% by weight relative to the total weight of the composition, where the fatty phase containing at least one liquid, solid or semi-solid fatty substance. The fatty substance includes, but is not limited to, oils, waxes, gums, and so-called pasty fatty substances. Alternatively, the compositions may be in the form of a stable dispersion such as a water-in-oil or oil-inwater emulsion. Additionally, the compositions may contain one or more conventional cosmetic or dermatological additives or adjuvants, including but not limited to, antioxidants, preserving agents, fillers, surfactants, UVA and/or UVB sunscreens, fragrances, thickeners, wetting agents and anionic, nonionic or amphoteric polymers, and dyes or

[0226] Emulsified cosmetics and quasi drugs which are producible with the use of emulsified materials comprising at least one silk protein of the present invention include, for example, cleansing cosmetics (beauty soap, facial wash, shampoo, rinse, and the like), hair care products (hair dye, hair cosmetics, and the like), basic cosmetics (general

cream, emulsion, shaving cream, conditioner, cologne, shaving lotion, cosmetic oil, facial mask, and the like), make-up cosmetics (foundation, eyebrow pencil, eye cream, eye shadow, mascara, and the like), aromatic cosmetics (perfume and the like), tanning and sunscreen cosmetics (tanning and sunscreen cream, tanning and sunscreen lotion, tanning and sunscreen oil, and the like), nail cosmetics (nail cream and the like), eyeliner cosmetics (eyeliner and the like), lip cosmetics (lipstick, lip cream, and the like), oral care products (tooth paste and the like) bath cosmetics (bath products and the like), and the like.

[0227] The cosmetic composition may also be in the form of products for nail care, such as a nail varnish. Nail varnishes are herein defined as compositions for the treatment and colouring of nails, comprising an effective amount of silk protein in a cosmetically acceptable medium. An effective amount of a silk protein for use in a nail varnish composition is herein defined as a proportion of from about  $10^{-4}$  to about 30% by weight relative to the total weight of the varnish. Components of a cosmetically acceptable medium for nail varnishes are described in U.S. Pat. No. 6,280,747. The nail varnish typically contains a solvent and a film forming substance, such as cellulose derivatives, polyvinyl derivatives, acrylic polymers or copolymers, vinyl copolymers and polyester polymers. The composition may also contain an organic or inorganic pigment.

[0228] Hair care compositions are herein defined as compositions for the treatment of hair, including but not limited to shampoos, conditioners, lotions, aerosols, gels, and mousses, comprising an effective amount of silk protein in a cosmetically acceptable medium. An effective amount of a silk protein for use in a hair care composition is herein defined as a proportion of from about  $10^{-2}$  to about 90% by weight relative to the total weight of the composition. Components of a cosmetically acceptable medium for hair care compositions are described in US 2004/0170590, U.S. Pat. No. 6,280,747, U.S. Pat. No. 6,139,851, and U.S. Pat. No. 6,013,250. For example, these hair care compositions can be aqueous, alcoholic or aqueous-alcoholic solutions, the alcohol preferably being ethanol or isopropanol, in a proportion of from about 1 to about 75% by weight relative to the total weight, for the aqueous-alcoholic solutions. Additionally, the hair care compositions may contain one or more conventional cosmetic or dermatological additives or adjuvants, as given above.

[0229] Hair colouring compositions are herein defined as compositions for the colouring, dyeing, or bleaching of hair, comprising an effective amount of silk protein in a cosmetically acceptable medium. An effective amount of a silk protein for use in a hair colouring composition is herein defined as a proportion of from about  $10^{-4}$  to about 60% by weight relative to the total weight of the composition. Components of a cosmetically acceptable medium for hair colouring compositions are described in US 2004/0170590, U.S. Pat. No. 6,398,821 and U.S. Pat. No. 6,129,770. For example, hair colouring compositions generally contain a mixture of inorganic peroxygen-based dye oxidizing agent and an oxidizable coloring agent. The peroxygen-based dye oxidizing agent is most commonly hydrogen peroxide. The oxidative hair coloring agents are formed by oxidative coupling of primary intermediates (for example p-phenylenediamines, p-aminophenols, p-diaminopyridines, hydroxyindoles, aminoindoles, aminothymidines, or cyanophenols) with secondary intermediates (for example phenols, resorcinols, m-aminophenols, m-phenylenediamines, naphthols, pyrazolones, hydroxyindoles, catechols or pyrazoles). Additionally, hair colouring compositions may contain oxidizing acids, sequestrants, stabilizers, thickeners, buffers carriers, surfactants, solvents, antioxidants, polymers, non-oxidative dyes and conditioners.

[0230] The silk proteins can also be used to coat pigments and cosmetic particles in order to improve dispersibility of the particles for use in cosmetics and coating compositions. Cosmetic particles are herein defined as particulate materials such as pigments or inert particles that are used in cosmetic compositions. Suitable pigments and cosmetic particles, include, but are not limited to, inorganic color pigments, organic pigments, and inert particles. The inorganic color pigments include, but are not limited to, titanium dioxide, zinc oxide, and oxides of iron, magnesium, cobalt, and aluminium. Organic pigments include, but are not limited to, D&C Red No. 36, D&C Orange No. 17, the calcium lakes of D&C Red Nos. 7, 11, 31 and 34, the barium lake of D&C Red No. 12, the strontium lake D&C Red No. 13, the aluminium lake of FD&C Yellow No. 5 and carbon black particles. Inert particles include, but are not limited to, calcium carbonate, aluminium silicate, calcium silicate, magnesium silicate, mica, talc, barium sulfate, calcium sulfate, powdered Nylon<sup>TM</sup>, perfluorinated alkanes, and other inert plastics.

[0231] The silk proteins may also be used in dental floss (see, for example, US 2005/0161058). The floss may be monofilament yarn or multifilament yarn, and the fibers may or may not be twisted. The dental floss may be packaged as individual pieces or in a roll with a cutter for cutting pieces to any desired length. The dental floss may be provided in a variety of shapes other than filaments, such as but not limited to, strips and sheets and the like. The floss may be coated with different materials, such as but not limited to, wax, polytetrafluoroethylene monofilament yarn for floss.

[0232] The silk proteins may also be used in soap (see, for example, US 2005/0130857).

# Pigment and Cosmetic Particle Coating

[0233] The effective amount of a silk protein for use in pigment and cosmetic particle coating is herein defined as a proportion of from about  $10^{-4}$  to about 50%, but preferably from about 0.25 to about 15% by weight relative to the dry weight of particle. The optimum amount of the silk protein to be used depends on the type of pigment or cosmetic particle being coated. For example, the amount of silk protein used with inorganic color pigments is preferably between about 0.01% and 20% by weight. In the case of organic pigments, the preferred amount of silk protein is between about 1% to about 15% by weight, while for inert particles, the preferred amount is between about 0.25% to about 3% by weight. Methods for the preparation of coated pigments and particles are described in U.S. Pat. No. 5,643, 672. These methods include: adding an aqueous solution of the silk protein to the particles while tumbling or mixing, forming a slurry of the silk protein and the particles and drying, spray drying a solution of the silk protein onto the particles or lyophilizing a slurry of the silk protein and the particles. These coated pigments and cosmetic particles may be used in cosmetic formulations, paints, inks and the like.

#### Biomedical

[0234] The silk proteins may be used as a coating on a bandage to promote wound healing. For this application, the

bandage material is coated with an effective amount of the silk protein. For the purpose of a wound-healing bandage, an effective amount of silk protein is herein defined as a proportion of from about 10<sup>-4</sup> to about 30% by weight relative to the weight of the bandage material. The material to be coated may be any soft, biologically inert, porous cloth or fiber. Examples include, but are not limited to, cotton, silk, rayon, acetate, acrylic, polyethylene, polyester, and combinations thereof. The coating of the cloth or fiber may be accomplished by a number of methods known in the art. For example, the material to be coated may be dipped into an aqueous solution containing the silk protein. Alternatively, the solution containing the silk protein may be sprayed onto the surface of the material to be coated using a spray gun. Additionally, the solution containing the silk protein may be coated onto the surface using a roller coat printing process. The wound bandage may include other additives including, but not limited to, disinfectants such as iodine, potassium iodide, povidon iodine, acrinol, hydrogen peroxide, benzalkonium chloride, and chlorohexidine; cure accelerating agents such as allantoin, dibucaine hydrochloride, and chlorophenylamine malate; vasoconstrictor agents such as naphazoline hydrochloride; astringent agents such as zinc oxide; and crust generating agents such as boric acid.

[0235] The silk proteins of the present invention may also be used in the form of a film as a wound dressing material. The use of silk proteins, in the form of an amorphous film, as a wound dressing material is described in U.S. Pat. No. 6,175,053. The amorphous film comprises a dense and nonporous film of a crystallinity below 10% which contains an effective amount of silk protein. For a film for wound care, an effective amount of silk protein is herein defined as between about 1 to 99% by weight. The film may also contain other components including but not limited to other proteins such as sericin, and disinfectants, cure accelerating agents, vasoconstrictor agents, astringent agents, and crust generating agents, as described above. Other proteins such as sericin may comprise 1 to 99% by weight of the composition. The amount of the other ingredients listed is preferably below a total of about 30% by weight, more preferably between about 0.5 to 20% by weight of the composition. The wound dressing film may be prepared by dissolving the above mentioned materials in an aqueous solution, removing insolubles by filtration or centrifugation, and casting the solution on a smooth solid surface such as an acrylic plate, followed by drying.

[0236] The silk proteins of the present invention may also be used in sutures (see, for example, US 2005/0055051). Such sutures can feature a braided jacket made of ultrahigh molecular weight fibers and silk fibers. The polyethylene provides strength. Polyester fibers may be woven with the high molecular weight polyethylene to provide improved tie down properties. The silk may be provided in a contrasting color to provide a trace for improved suture recognition and identification. Silk also is more tissue compliant than other fibers, allowing the ends to be cut close to the knot without concern for deleterious interaction between the ends of the suture and surrounding tissue. Handling properties of the high strength suture also can be enhanced using various materials to coat the suture. The suture advantageously has the strength of Ethibond No. 5 suture, yet has the diameter, feel and tie-ability of No. 2 suture. As a result, the suture is ideal for most orthopedic procedures such as rotator cuff repair, Achilles tendon repair, patellar tendon repair, ACL/ PCL reconstruction, hip and shoulder reconstruction procedures, and replacement for suture used in or with suture anchors. The suture can be uncoated, or coated with wax (beeswax, petroleum wax, polyethylene wax, or others), silicone (Dow Corning silicone fluid 202A or others), silicone rubbers, PBA (polybutylate acid), ethyl cellulose (Filodel) or other coatings, to improve lubricity of the braid, knot security, or abrasion resistance, for example.

[0237] The silk proteins of the present invention may also be used in stents (see, for example, US 2004/0199241). For example, a stent graft is provided that includes an endoluminal stent and a graft, wherein the stent graft includes silk. The silk induces a response in a host who receives the stent graft, where the response can lead to enhanced adhesion between the silk stent graft and the host's tissue that is adjacent to the silk of the silk stent graft. The silk may be attached to the graft by any of various means, e.g., by interweaving the silk into the graft or by adhering the silk to the graft (e.g., by means of an adhesive or by means of suture). The silk may be in the form of a thread, a braid, a sheet, powder, etc. As for the location of the silk on the stent graft, the silk may be attached only the exterior of the stent, and/or the silk may be attached to distal regions of the stent graft, in order to assist in securing those distal regions to neighbouring tissue in the host. A wide variety of stent grafts may be utilized within the context of the present invention, depending on the site and nature of treatment desired. Stent grafts may be, for example, bifurcated or tube grafts, cylindrical or tapered, self-expandable or balloon-expandable, unibody or, modular, etc.

[0238] In addition to silk, the stent graft may contain a coating on some or all of the silk, where the coating degrades upon insertion of the stent graft into a host, the coating thereby delaying contact between the silk and the host. Suitable coatings include, without limitation, gelatin, degradable polyesters (e.g., PLGA, PLA, MePEG-PLGA, PLGA-PEG-PLGA, and copolymers and blends thereof), cellulose and cellulose derivatives (e.g., hydroxypropyl cellulose), polysaccharides (e.g., hyaluronic acid, dextran, dextran sulfate, chitosan), lipids, fatty acids, sugar esters, nucleic acid esters, polyanhydrides, polyorthoesters and polyvinylalcohol (PVA). The silk-containing stent grafts may contain a biologically active agent (drug), where the agent is released from the stent graft and then induces an enhanced cellular response (e.g., cellular or extracellular matrix deposition) and/or fibrotic response in a host into which the stent graft has been inserted.

[0239] The silk proteins of the present invention may also be used in a matrix for producing ligaments and tendons ex vivo (see, for example, US 2005/0089552). A silk-fiberbased matrix can be seeded with pluripotent cells, such as bone marrow stromal cells (BMSCs). The bioengineered ligament or tendon is advantageously characterized by a cellular orientation and/or matrix crimp pattern in the direction of applied mechanical forces, and also by the production of ligament and tendon specific markers including collagen type I, collagen type III, and fibronectin proteins along the axis of mechanical load produced by the mechanical forces or stimulation, if such forces are applied. In a preferred embodiment, the ligament or tendon is characterized by the presence of fiber bundles which are arranged into a helical organization. Some examples of ligaments or tendons that can be produced include anterior cruciate ligament, posterior cruciate ligament, rotator cuff tendons, medial collateral

ligament of the elbow and knee, flexor tendons of the hand, lateral ligaments of the ankle and tendons and ligaments of the jaw or temporomandibular joint. Other tissues that may be produced by methods of the present invention include cartilage (both articular and meniscal), bone, muscle, skin and blood vessels.

[0240] The silk proteins of the present invention may also be used in hydrogels (see, for example, US 2005/0266992). Silk fibroin hydrogels can be characterized by an open pore structure which allows their use as tissue engineering scaffolds, substrate for cell culture, wound and burn dressing, soft tissue substitutes, bone filler, and as well as support for pharmaceutical or biologically active compounds.

[0241] The silk proteins may also be used in dermatological compositions (see, for example, US 2005/0019297). Furthermore, the silk proteins of the invention and derivatives thereof may also be used in sustained release compositions (see, for example, US 2004/0005363).

### **Textiles**

[0242] The silk proteins of the present invention may also be applied to the surface of fibers for subsequent use in textiles. This provides a monolayer of the protein film on the fiber, resulting in a smooth finish. U.S. Pat. No. 6,416,558 and U.S. Pat. No. 5,232,611 describe the addition of a finishing coat to fibers. The methods described in these disclosures provide examples of the versatility of finishing the fiber to provide a good feel and a smooth surface. For this application, the fiber is coated with an effective amount of the silk protein. For the purpose of fiber coating for use in textiles, an effective amount of silk protein is herein defined as a proportion of from about 1 to about 99% by weight relative to the weight of the fiber material. The fiber materials include, but are not limited to textile fibers of cotton, polyesters such as rayon and Lycra<sup>TM</sup>, nylon, wool, and other natural fibers including native silk. Compositions suitable for applying the silk protein onto the fiber may include co-solvents such as ethanol, isopropanol, hexafluoranols, isothiocyanouranates, and other polar solvents that can be mixed with water to form solutions or microemulsions. The silk protein-containing solution may be sprayed onto the fiber or the fiber may be dipped into the solution. While not necessary, flash drying of the coated material is preferred. An alternative protocol is to apply the silk protein composition onto woven fibers. An ideal embodiment of this application is the use of silk proteins to coat stretchable weaves such as used for stockings.

# Composite Materials

[0243] Silk fibres can be added to polyurethane, other resins or thermoplastic fillers to prepare panel boards and other construction material or as moulded furniture and benchtops that replace wood and particle board. The composites can be also be used in building and automotive construction especially rooftops and door panels. The silk fibres re-enforce the resin making the material much stronger and allowing lighterweight construction which is of equal or superior strength to other particle boards and composite materials. Silk fibres may be isolated and added to a synthetic composite-forming resin or be used in combination with plant-derived proteins, starch and oils to produce a biologically-based composite materials. Processes for the production of such materials are described in JP

2004284246, US 2005175825, U.S. Pat. No. 4,515,737, JP 47020312 and WO 2005/017004.

# Paper Additives

**[0244]** The fibre properties of the silk of the invention can add strength and quality texture to paper making. Silk papers are made by mottling silk threads in cotton pulp to prepare extra smooth handmade papers is used for gift wrapping, notebook covers, carry bags. Processes for production of paper products which can include silk proteins of the invention are generally described in JP 2000139755.

#### Advanced Materials

[0245] Silks of the invention have considerable toughness and stands out among other silks in maintaining these properties when wet (Hepburn et al., 1979).

[0246] Areas of substantial growth in the clothing textile industry are the technical and intelligent textiles. There is a rising demand for healthy, high value functional, environmentally friendly and personalized textile products. Fibers, such as those of the invention, that do not change properties when wet and in particular maintain their strength and extensibility are useful for functional clothing for sports and leisure wear as well as work wear and protective clothing. [0247] Developments in the weapons and surveillance technologies are prompting innovations in individual protection equipments and battle-field related systems and structures. Besides conventional requirements such as material durability to prolonged exposure, heavy wear and protection from external environment, silk textiles of the invention can be processed to resist ballistic projectiles, fire and chemicals. Processes for the production of such materials are described in WO 2005/045122 and US 2005268443.

# **EXAMPLES**

#### Example 1

Preparation and Analysis of Late Last Instar Salivary Eland cDNAs

[0248] The proteins that are found in euaculeatan and neuropteran (Apis mellifera, Bombus terrestris, Myrmecia forficata, Oecophylla smaragdina, Mallada signata) silks were identified by matching ion trap consecutive mass spectral (MS/MS) fragmentation patterns of peptides obtained by trypsin digestion of the silk with the predicted mass spectral data of proteins encoded by cDNAs isolated from the salivary gland of late final instar larvae. For confirmation that no proteins were missed by this analysis for the honeybee, the peptide mass spectral data were also compared to virtual tryptic digests of Apis mellifera proteins predicted by the bee genome project and translations of the Amel3 honeybee genomic sequences in all six reading frames.

## Honeybee

[0249] Apis mellifera larvae were obtained from domestic hives. Previously it was shown that silk production in Apis mellifera is confined to the salivary gland during the latter half of the final instar (Silva-Zacarin et al., 2003). During this period, RNA is more abundant in the posterior end of the gland (Flower and Kenchington, 1967). The cubical cell regions of 50 salivary glands were dissected from late fifth

instar *Apis mellifera* immersed in phosphate buffered saline. The posterior end of the dissected gland was immediately placed into RNAlater® (Ambion, Austin, Tex., USA), to stabilise the mRNA, and subsequently stored at 4° C.

[0250] Total RNA (35 µg) was isolated from the late final instar salivary glands using the RNAqueous for PCR kit from Ambion (Austin, Tex., USA). Message RNA was isolated from the total RNA using the Micro-FastTrack<sup>TM</sup> 2.0 mRNA Isolation kit from Invitrogen (Calsbad, Calif., USA) according to the manufacturer's directions with the isolated mRNA being eluted into 10 ul RNAse free water. [0251] A cDNA library was constructed from the mRNA isolated from Apis mellifera larvae using the CloneMiner<sup>TM</sup> cDNA library construction kit of Invitrogen (Calsbad, Calif., USA) with the following modifications from the standard protocol: For the first strand synthesis, 0.5 µl of BiotinattB2-Oligo(dT) primer at 6 pmol µl<sup>-1</sup> and 0.5 µl of dNTPs at 2 mM each was added to the 10 µl mRNA. After incubation at 65° C. for 5 min then 45° C. for 2 min, 2 µl 5× First strand buffer, 1 µl of 0.1M DTT, and 0.5 µl Super-Script™ II RT at 200 U·µl<sup>-1</sup> were added. For second strand synthesis, the total volume of all reagents was halved and after ethanol precipitation, the cDNA was resuspended in 5 μl of DEPC-treated water. The aatB1 adapter (1 μl) was ligated in a total volume of 10 µl to the 5 µl cDNA with 2 ul 5× Adapter buffer, 1 ul 0.1M DTT and 1 ul T4 DNA ligase (1 U·μl<sup>-1</sup>) at 16° C. for 48 hrs with an additional 0.5 μl T4 DNA ligase (1 U µl<sup>-1</sup>) added after 16 hrs. The cDNA was size fractionated according to the manufactures instructions with samples eluting between 300-500 µl being precipitated with ethanol, resuspended and transformed into the provided *E. coli* DH10B<sup>TM</sup> T1 phage resistant cells as recommended. The cDNA library comprised approximately 1,200,000 colony forming units (cfu) with approximately 1% the original vector. The average insert size was 1.3±1.4 kbp. [0252] Eighty two clones were randomly selected and sequenced using the GenomeLab<sup>TM</sup> DTCS Quick start kit (BeckmanCoulter, Fullerton Calif. USA) and run on a CEQ8000 Biorad sequencer. These clustered into fifty four groups (Table 2). Identification of the cDNAs that encoded the silk proteins is described below.

# Other Species

[0253] Total RNA was isolated from 4 bumblebee (Bombus terrestris) (2 µg RNA), 4 bulldog ant (Myrmecia forficata) (3 µg RNA), approximately 100 Weaver ants (Oecophylla smaragdina) (0.4 µg RNA) and approximately 50 green lacewing (Mallada signata) late larval labial glands using the RNAqueous for PCR kit from Ambion (Austin, Tex., USA). mRNA was isolated from the total RNA using the Micro-FastTrack<sup>TM</sup> 2.0 mRNA Isolation kit from Invitrogen (Calsbad, Calif., USA) into a final volume of 10 μl water. cDNA libraries were constructed from the mRNA using the CloneMiner<sup>TM</sup> cDNA kit of Invitrogen (Calsbad, Calif., USA) with the following modifications from the standard protocol: For the first strand synthesis, 3 pmol of Biotin-attB2-Oligo(dT) primer and 1 nmol each dNTPs were added to the 10 µl mRNA. After 5 min at 65° C. followed by 2 min at 45° C., 2 dl 5× First strand buffer, 50 nmol DTT, and 100 U SuperScript<sup>TM</sup> II RT were added.

TABLE 2

A. mellifera final instar salivary gland cDNAs and MS ion trap fragmentation patterns of peptides from trypsin digestion of SDS treated brood comb silk.										
Number of cDNA's in cluster	Abundance in salivary gland library (%)	Protein or gene synonyms	Number of tryptic peptides identified in the silk		Coverage of protein sequence (% protein)	Protein identification				
Proteins identified in cDNA library and in honeybee silk										
10	13	Xenosin; GB15233-PA	9	143.89	25	AC004701				
8	11	Xenospira1; GB12184-PA	10	165.13	37	No matches				
6	7	Xenospira4; GB19585-PA	8	142.16	35	No matches				
6	7	Xenospira2; GB12348-PA	9	145.91	28	No matches				
5	6	Xenospira3; GB17818-PA	9	147.02	31	No matches				
		Proteins identif	ied in cDNA	library on	ly					
4 2	4 2	GB14261-PA Contig 2504	0							
2	2	GB17108-PA	Ö							
1	1	Contig 68	Ö							
1	1	Contig 110	0							
1	1	Contig 487	0							
1	1	GB14199-PA	0							
1	1	GB10847-PA	0							
1	1	Contig 1047	0							
1	1	GB17558-PA	0							
1	1	Contig 1471	0							
1	1	GB16480-PA	0							
1	1	Contig 1818	0							
1	1	GB16911-PA	0							
1	1	Contig 2046	0							

TABLE 2-continued

		instar salivary gl des from trypsin				
Number of cDNA's in cluster	Abundance in salivary gland library (%)	Protein or gene synonyms	Number of tryptic peptides identified in the silk	Distinct summed MS/MS search score	Coverage of protein sequence (% protein)	Protein identification
1	1	Contig 2136	0			
1	1	Contig 2196	0			
1	1	GB11234-PA	0			
1	1	GB11199-PA	0			
1	1	GB18183-PA	0			
1	1	Contig 2938	0			
1	1	Contig 2976	0			
1	1	Contig 3263	0			
1	1	Contig 3527	0			
1	1	GB16412-PA	0			
1	1	GB18750-PA	0			
1	1	GB16132-PA	0			
1	1	Contig 4536	0			
1	1	GB19431-PA	0			
1	1	Contig 4704	0			
1	1	Contig 4758	0			
1	1	Contig 4830	0			
1	1	Contig 4968	0			
1	1	Contig 5402	0			
1	1	Contig 5971	0			
1	1	GB11274-PA	0			
1	1	GB14693-PA	0			
1	1	GB19585-PA	0			
1	1	GB15606-PA	0			
1	1	GB16801-PA	0			
1	1	GB12085-PA	0			
1	1	Contig 7704	0			
1	1	Contig 8630	0			
1	1	Contig 9774	0			
1	1	GB16452-PA	0			
1	1	GB10420-PA	0			
1	1	GB14724-PA	0			

[0254] For second strand synthesis, the total volume of all reagents was halved from the manufacturer's recommended amounts and after ethanol precipitation, the cDNA was resuspended in 5  $\mu l$  of DEPC-treated water. The aatB1 adapter (1  $\mu l$ ) was ligated in a total volume of 10  $\mu l$  to the 5  $\mu l$  cDNA with 2  $\mu l$  5× Adapter buffer, 50 nmol DTT and 1 U T4 DNA ligase at 16° C. for 12 hrs. The cDNA libraries comprised approximately  $2.4\times10^7$  (bumblebee),  $5.0\times10^7$  (bulldog ant) and 6000 (green ant) colony forming units (cfu) with less than 1% the original vector for the bulldog ant and bumblebee libraries and greater than 80% original

vector in the green ant library. The average insert size within the libraries was 1.3 Kbp.

[0255] Sequence data was obtained from more than 100 random clones from the cDNA libraries from bumblebee and bulldog ant, 82 clones from the honeybee and 60 clones from the lacewing. The technical difficulties of obtaining salivary glands from the minute green ants (approximately 1 mm in length) reduced the efficiency of the library from this species and as such only 40 sequences were examined. A summary of the silk proteins identified is provided in Table 3

TABLE 3

	Identifica	tion and pr	operties c	of the euaculeata	n silk protein	S.
Species	Protein name	Length of protein (amino acids)	% cDNA library clones	Distinct summed MS/MS identification score	% helical structure**	MARCOIL predicted coiled coil length*** (amino acids)
Honeybee	AmelF1*	333	6	52	76	117
Honeybee	AmelF2*	290	7	51	88	175
Honeybee	AmelF3*	335	11	107	81	154
Honeybee	AmelF4*	342	7	88	76	174
Honeybee	AmelSA1*	578	13	40	41	45
Bumblebee	BBF1	327	4	180	86	147
Bumblebee	BBF2	313	14	100	84	199
Bumblebee	BBF3	332	20	218	86	146

TABLE 3-continued

	Identification and properties of the euaculeatan silk proteins.									
Species	Protein name	Length of protein (amino acids)	% cDNA library clones	Distinct summed MS/MS identification score	% helical structure**	MARCOIL predicted coiled coil length*** (amino acids)				
Bumblebee	BBF4	357	32	137	80	188				
Bumblebee	BBSA1	>501	3	138	21	0				
Bulldog ant	BAF1	422	16	99	69	121				
Bulldog ant	BAF2	411	30	90	76	132				
Bulldog ant	BAF3	394	26	88	79	131				
Bulldog ant	BAF4	441	24	116	76	157				
Weaver ant	GAF1	391	35	228	74	177				
Weaver ant	GAF2	400	22	191	79	158				
Weaver ant	GAF3	395	13	156	72	103				
Weaver ant	GAF4	443	17	148	74	166				
Lacewing	MalF1	596	23	45	89	151				

<sup>\*</sup>also referred to herein as Xenospira1-4 and Xenosin respectively,

#### Example 2

Preparation and Proteomic Analysis of Native Silk

[0256] Honeybee brood comb after the removal of larvae, bumblebee cocoons after the removal of larvae, bulldog ant cocoons after the removal of larvae, or weaver ant silk sheets were washed extensively three times in warm water to remove water soluble contaminants and then washed extensively three times in chloroform to remove wax. Chloroform was removed by rinsing in distilled water and a subset of this silk was retained for analysis. A subset of the Hymenopteran (ants and bees) silk samples was further washed by boiling for 30 minutes in 0.05% sodium carbonate solution, a standard procedure for degumming silkworm silk, then rinsed in distilled water. Lacewing silk was rinsed in distilled water only. A subset of the lacewing silk samples was degummed by boiling for 30 minutes in 0.05% sodium carbonate solution.

[0257] A subset of the honeybee material was soaked overnight in 2% SDS at 95° C., followed by three washes in distilled water. Extraction in hot SDS solution solubilises most proteins, but in this case the silk sheets retained their conformation.

[0258] The clean silks were analysed by liquid chromatography followed by tandem mass spectrometry (LCMS) as described below.

[0259] Pieces of cleaned silk were placed in a well of a Millipore 'zipplate', a 96 well microtitre tray containing a plug of C18 reversed phase chromatography medium through the bottom of each well to which was added 20  $\mu$ l 25 mM ammonium bicarbonate containing 160 ng of sequencing grade trypsin (Promega). Then the tray was incubated overnight in a humidified plastic bag at 30° C.

[0260] The C18 material was wetted by pipetting acetonitrile (10  $\mu l)$  to the sides of each well and incubating the plate at 37° C. for 15 min. Formic acid solution (130  $\mu l,~1\%~v/v)$  was added to each well and after 30 min peptides from the digested bee proteins were captured on the C18 material by slowly drawing the solutions from each well through the base of the plate under a reduced vacuum. The C18 material was washed twice by drawing through 100  $\mu l$  of formic acid solution. Peptides were eluted with 6  $\mu l$  of 1% formic acid

in 70% methanol pipetted directly onto the C18 material and promptly centrifuged through the C18 plug to an underlying microtitre tray. This tray was placed under vacuum till the volume in each well was reduced about 2-fold by evaporation. Formic acid solution (10  $\mu$ l) was added to each well and the tray was transferred to the well plate sampler of an Agilent 1100 capillary liquid chromatography system.

[0261] Peptides (8 µl) from the silk extract were bound to an Agilent Zorbax SB-C18 5 µm 150×0.5 mm column with a flow rate of 0.1% formic acid/5% acetonitrile at 20  $\mu l \cdot min^{-1}$  for one min then eluted with gradients of increasing acetonitrile concentration to 0.1% formic acid/20% acetonitrile over one minute at 5  $\mu l \cdot min^{-1}$ , then to 0.1% formic acid/50% acetonitrile over 28 minutes, then to 0.1% formic acid/95% acetonitrile over one minute. The column was washed with 0.1% formic acid/95%-100% acetonitrile over 5 mins at 20  $\mu l \cdot min^{-1}$  and reequilibrated with 0.1% formic acid/5% acetonitrile for 7 mins before peptides from the next well were sampled.

[0262] Eluate from the column was introduced to an Agilent XCT ion trap mass spectrometer through the instrument's electrospray ion source fitted with a micronebuliser. Briefly, as peptides were eluting from the column, the ion trap collected full spectrum positive ion scans (100-2200 m/z) followed by two MS/MS scans of ions observed in the full spectrum avoiding the selection of ions that carried only a single charge. When an ion was selected for MS/MS analysis all others were excluded from the ion trap, the selected ion was fragmented according to the instrument's recommended "SmartFrag" and "Peptide Scan" settings. Once two fragmentation spectra were collected for any particular m/z value it was excluded from selection for analysis for a further 30 seconds to avoid collecting redundant data.

[0263] Mass spectral data sets from the entire experiment were analysed using Agilent's Spectrum Mill software to match the data with predictions of protein sequences from the cDNA libraries. The software generated scores for the quality of each match between experimentally observed sets of masses of fragments of peptides and the predictions of fragments that might be generated according to the sequences of proteins in a provided database. All the

<sup>\*\*</sup>predicted by PROFsec,

<sup>\*\*\*</sup>predicted by MARCOIL at 90% threshold

sequence matches reported here received scores greater than 20, the default setting for automatic, confident acceptance of valid matches.

[0264] This analysis identified that five proteins expressed at high levels in the labial gland matched the silk from each of the cognate bee species (shown in Tables 2 and 3) and four proteins expressed at high levels in the labial gland matched the silk from each of the cognate ant species (shown in Table 3). The abundance of message RNA encoding these proteins in the labial gland of the larvae was consistent with the proteins being abundantly produced (abundance of message shown in Table 3).

[0265] To ensure that none of the honeybee silk proteins were missed by this identification process, we also compared the honeybee silk trypsin peptide mass spectral data to a set of publicly available predicted protein sequences from the honeybee genome project, generated by a computer algorithm that tries to recognise transcribed genes in the complete genomic DNA sequences of the bee. Additionally, we generated a database of translations in the six possible reading frames of each contiguous genomic DNA sequence provided by the bee genome project (Amel3 release). These translated DNA sequences were presented to the Spectrum Mill software as if they were the sequences of very large proteins. Matching MS/MS peptide data identified open reading frames within the genomic sequences that had encoded parts of the isolated bee proteins without the need to first predict the organisation of genes. No additional proteins were identified in the silk by this analysis.

# Example 3

# Structural Analysis of the Native Silk

[0266] Native silk samples were prepared as described in Example 2. Silk samples were examined using a Bruker Tensor 37 Fourier transform infrared spectrometer with a Pike Miracle diamond attenuated total reflection accessory. Analysis of the amide I and II regions of the spectra of honeybee, bumblebee, green ant, bulldog ant silks and lacewing larval silk (FIG. 1) shows that all these silks have a predominantly alpha-helical secondary structure. The silks of the Euaculeatan species have dominant peaks in the FT-IR spectra at 1645-1646 cm<sup>-1</sup>, shifted approximately 10 cm<sup>-1</sup> lower than a classical  $\alpha$ -helical signal and broadened. This shift in the  $\alpha$ -helical signal is typical of coiled-coil proteins (Heimburg et al., 1999). Spectra from samples that were degummed were unchanged.

#### Example 4

The Amino Acid Composition of Native Silks Closely Resembles that of the Identified Silk Proteins

[0267] The amino acid composition of the native silks was determined after 24 hr gas phase hydrolysis at 110° C. using the Waters AccQTag chemistry by Australian Proteome Analysis Facility Ltd (Macquarie University, Sydney).

[0268] The measured amino acid composition of the SDS washed silk was similar to that predicted from the identified silks protein sequences (FIGS. 2 and 3).

#### Example 5

#### Structural Analysis of the Silk Proteins

Predicted Secretory Peptides

**[0269]** As expected for silk proteins, the SignalP 3.0 signal prediction program (Bendtsen et al., 2004), which uses two models to identify signal peptides predicted that all the identified silk genes encoded proteins which contain signal peptides that targeted them for secretion from a cell (data not shown). The predicted cleavage sites of the polypeptides are as follows:

[0270] Xenospira1 (AmelF1)—between pos 19 and 20 (ASA-GL),

[0271] Xenospira2 (AmelF2)—between pos 19 and 20 (AEG-RV),

[0272] Xenospira3 (AmelF3)—between pos 19 and 20 (VHA-GV),

[0273] Xenospira4 (AmelF4)—between pos 19 and 20 (ASG-AR),

[0274] Xenosin (AmelSA1)—between pos 19 and 20 (VCA-GV),

[0275] BBF1—between pos 19 and 20 (ASA-GQ),

[0276] BBF2—between pos 20 and 21 (AEG-HV),

[0277] BBF3—between pos 19 and 20 (VHA-GS),

[0278] BBF4—between pos 19 and 20 (ASA-GK),

[0279] BAF1—between pos 19 and 20 (ASA-SG),

[0280] BAF2—between pos 19 and 20 (ASG-RV),

 $\hbox{\hbox{$[0281]$}}\quad BAF3--between pos\ 19\ and\ 20\ (ASG-NL),$ 

[0282] BAF4—between pos 19 and 20 (VGA-SE),

[0283] GAF1—between pos 19 and 20 (ADA-SK),

[0284] GAF2—between pos 19 and 20 (ASG-GV), [0285] GAF3—between pos 19 and 20 (ASG-GV),

[0286] GAF4—between pos 19 and 20 (VGA-SE),

[0287] MalF1—between pos 26 and 27 (SST-AV).

All Four of the Ant and Four of the Five Bee Silk Proteins are Helical and Formed Coiled Coils

[0288] Protein modelling and results from pattern recognition algorithms confirmed that the majority of the identified honeybee silk proteins were helical proteins that formed coiled coils.

[0289] PROFsec (Rost and Sander, 1993) and NNPredict (McClelland and Rumelhart, 1988; Kneller et al., 1990), algorithms were used to investigate the secondary structure of the identified silk genes. These algorithms identified Xenospira1 [GB12184-PA](SEQ ID NO:1), Xenospira2 [GB12348-PA] (SEQ ID NO:3), Xenospira3 [GB17818-PA] (SEQ ID NO:5), and Xenospira4 [GB19585-PA] (SEQ ID NO:7), as highly helical proteins, with between 76-85% helical structure (Table 4). Xenosin [GB15233-PA](SEQ ID NO:10) had significantly less helical structure.

TABLE 4

The secondary structure of *Apis mellifera* silk proteins predicted by PROFsec (Rost and Sander, 1993) showing percentages of helices, extended sheets and loops.

	helical		exte	nded	loop		
Protein	PROFsec	NNPredict	PROFsec	NNPredict	PROFsec	NNPredict	
Xenospira3	77	70	3	6	20	27	
Xenospira4	85	82	2	6	14	16	
Xenospira1	80	73	1	4	19	26	
Xenospira2	77	69	2	5	21	29	
Xenosin	41	41	8	9	51	50	

[0290] Further protein modelling and results from pattern recognition algorithms confirmed that the majority of the identified silk proteins were helical proteins that formed coiled coils. PredictProtein (Rost et al., 2004) algorithms were used to investigate the secondary structure of the identified silk genes. These algorithms identified Xenospira1 (SEQ ID NO:1), Xenospira2 (SEQ ID NO:3), Xenospira3 (SEQ ID NO:5), Xenospira4 (SEQ ID NO:7), BBF1 (SEQ ID NO:22), BBF2 (SEQ ID NO:24), BBF3 (SEQ ID NO:26), BBF4 (SEQ ID NO:28), BAF1 (SEQ ID NO:40), BAF2 (SEQ ID NO:42), BAF3 (SEQ ID NO:44), BAF4 (SEO ID NO:46), GAF1 (SEO ID NO:56), GAF2 (SEO ID NO:58), GAF3 (SEQ ID NO:60), GAF4 (SEQ ID NO:62), and MalF1 (SEQ ID NO:72) as highly helical proteins, with between 69-88% helical structure (Table 3). AmelSA1 [GB15233-PA] (Xenosin) (SEQ ID NO:10) and BBSA1 (SEQ ID NO:30) had significantly less helical structure.

[0291] Super-coiling of helical proteins (coiled coils) arises from a characteristic heptad repeat sequence normally denoted as  $(abcdefg)_n$  with generally hydrophobic residues in position a and d, and generally charged or polar residues at the remaining positions. The pattern recognition programs (MARCOIL (Delorenzi and Speed, 2002), COILS (Lupas et al., 1991)) identified numerous heptad repeats typical of coiled-coils in Xenospira1 [GB12184-PA] (SEQ ID NO:1), Xenospira2 [GB12348-PA] (SEQ ID NO:3), Xenospira3 [GB17818-PA] (SEQ ID NO:5), and Xenospira4 [GB19585-PA](SEQ ID NO:7) (MARCOIL: Table 5; COILS: FIG. 4), as well as BBF1 (SEQ ID NO:22), BBF2 (SEQ ID NO:24), BBF3 (SEQ ID NO:26), BBF4 (SEQ ID NO:28), BAF1 (SEQ ID NO:40), BAF2 (SEQ ID NO:42), BAF3 (SEQ ID NO:44), BAF4 (SEQ ID NO:46), GAF1 (SEQ ID NO:56), GAF2 (SEQ ID NO:58), GAF3 (SEQ ID NO:60), GAF4 (SEQ ID NO:62), and MalF1 (SEQ ID NO:72) (MARCOIL: Table 3).

Identification of a Novel Coiled Coil Sequence in the Honeybee Silk Proteins

[0292] The heptad repeats of amino acid residues identified in the sequences of Xenospira1 [GB12184-PA], Xenospira2 [GB12348-PA], Xenospira3 [GB17818-PA], Xenospira4 [GB19585-PA], were each highly indicative of a coiled coil secondary structure (FIG. 5) (see Table 5 for confidence levels). The fact that the heptads are found consecutively and numerously suggests the proteins adopt a very regular structure. Overlapping heptads were identified in two of the honeybee proteins: the major coiled coil region of Xenospira1 contained overlapping heptads with a 3 residue offset followed by a space of 5 residues and then four consecutive heptads; and the entire coiled coil region of

Xenospira2 had multiple overlapping heptads with a single offset and 4 residue offset (equivalent to 3 residue offset). The composition of amino acids in the various positions of the major heptad are shown in the first column in Table 6, with the positions of the overlapping heptads indicated in adjacent columns.

TABLE 5

Percent of residues in the identified silk proteins predicted to exist as coiled coil by the MARCOIL (Delorenzi and Speed, 2002) pattern recognition algorithm.

	Length of mature protein	Percent pro	otein that exists a	as coiled coil
Protein	(amino acids)	50% threshold	90% threshold	99% threshold
Xenospira3	315	64% (residues 68 to 268)	34% (residues 128- 223 and 235- 246)	20% (residues 149- 211)
Xenospira4	290	73% (residues 83- 293)	60% (residues 98- 168 and 182- 2.85)	27% (residues 113- 154 and 212- 247)
Xenospira1	316	69% (residues 67- 282)	49% (residues 103- 256)	18% (residues 113-
Xenospira2	328	65% (residues 89- 298)	54% (residues 110- 283)	45% (residues 127- 270)
Xenosin	350	26% (residues 32- 127)	9% (residues 42- 75)	2% (residues 59- 67)

[0293] Surprisingly the major heptads have a novel composition when viewed collectively—with an unusually high abundance of alanine in the 'hydrophobic' heptad positions a and d (see Table 6 and FIG. 5). Additionally, a high proportion of heptads have alanine at both a and d positions within the same heptad (33% in Xenospira1 [GB12184-PA]; 36% in Xenospira2 [GB12348-PA]; 27% in Xenospira3 [GB17818-PA]; and 38% in Xenospira4 [GB19585-PA]; see Tables 6 and 7).

TABLE 6

Summary of the number of each amino acid residues in the various heptad positions in coiled coil regions of honeybee silk

								р	rot	eins	١.							
								Χe	enos	pir.	a4							
	A	I	R	L	K	Т	E	V	F	S	Q	И	D	G	M	Y	W	Total
a	23	0	1	1	0	1	1	1	0	1	0	0	0	0	0	0	0	29
b	12	0	0	2	2	2	3	1	0	3	1	1	1	1	0	0	0	29
C	12	0	0	1	5	1	3	1	0	3	1	1	0	1	0	0	0	29
d	17	0	0	5	1	0	1	2	0	2	1	0	0	0	0	0	0	29
e f	12 13	0 1	1	0 1	0	2	4 7	2 1	0	5 1	2 1	1 2	0	0	0	0	0	29 29
g	9	3	4	0	2	1	2	1	0	2	0	1	2	2	0	0	0	29
								Χe	enos	pir.	a3							
	Α	I	R	L	K	Т	E	V	F	S	Q	N	D	G	M	Y	W	Total
a	19	0	0	1	0	4	2	0	0	1	1	1	0	0	0	1	0	30
b	8	0	0	5	1	2	2	0	0	5	4	2	1	0	0	0	0	30
C	13	0	1	0	3	2	2	3	0	1	2	0	1	1	0	0	1	30
d	13	3	0	2	2	0	2	2	0	4	0	1	1	0	0	0	0	30
e	8	0	0	2	2	2	4	0	0	7	4	0	0	1	0	0	0	30
f	7	0	2	3	4	2	4	0	0	4	1	2	1	0	0	0	0	30
g	9	0	5	2	3	0	1	2	0	5	0	2	1	0	0	0	0	30
	_	_	_			_	_		enos				_	~				m . 3
	A	Ι	R	L	K	Т	E	V	F	S	Q	И	D	G	M	Y	W	Total
a	20	0	0	1	0	3	1	1	1	1	0	0	0	0	0	0	0	28
b	7	2	2	2	2	2	2	4	0	1	1	3	0	0	0	0	0	28
C	9	0	2	0	4	1	2	4	0	1	3	2	0	0	1	1	1	28
d e	16 11	0	0	3	3	1	0 4	1	0	1	2	0	1 1	0	0	0	0	28 28
f	10	2	1	0	1	2	6	1	0	3	1	1	0	0	0	0	0	28
g	3	4	1	0	1	1	5	ō	0	0	2	4	o	1	1	0	0	28
_								Χe	enos	pir.	a1							
	A	I	R	L	K	Т	E	V	F	s	Q	N	D	G	M	Y	W	Total
a	13	3	0	1	2	0	1	1	0	2	1	1	0	2	0	0	0	27
b	7	1	1	1	6	0	2	1	0	3	1	0	4	0	0	0	0	27
C	8	1	2	1	1	1	7	2	0	1	1	1	0	1	0	0	0	27
d	18	0	0	2	1	2	1		0	2	1	0	0	0	0	0	0	27
e	11	1	2	1	1	2	3	2	0	4	0	0	0	0	0	0	0	27
f	7	0	3	0	2	1	3	3	0	7	0	1	0	0	0	0	0	27
g	13	0	0	3	3	0	2	1	0	3	1	0	0	0	1	0	0	27

TABLE 7

	Summary of	alanine res	idues in he	eptads of l	noneybee	silk proteins.	
Protein	Amount of helical structure (%)1	Number of major heptads	Amount of protein in major heptad (%)	Amount of Ala in major heptads (%)	Amount of Ala in position a of major heptads (%)	Amount of Ala in position d of major heptads (%)	Amount of Ala in position a and d of major heptads (%)
Xenospira1 Xenospira2	77 (70) 85 (82)	27 28		41 37	44 71	74 57	33 36
Xenospira3	80 (73)	30		37	63	43	27
Xenospira4	77 (69)	29		48	79	58	38
Xenosin	41 (41)			n/a	n/a	n/a	n/a

<sup>1</sup>PROFsec predictions with NNPredict predictions shown in brackets.

[0294] The composition of amino acids in the various heptad positions in the coiled coil region of the hymenopteran silks are summarised in FIGS. 6 and 7. As noted above, the positions within the heptads have a novel composition—the 'hydrophobic' heptad positions a and d of

the bee and ant silks contain very high levels of alanine (average 58%) and high levels of small polar residues (average 21%) in comparison to other coiled coils. Additionally, position e is unusually small and hydrophobic (Table 8, FIG. 7). Topographically this position is located

adjacent to the a residues within the helices. Its compositional similarity with the a and d residues suggest that the silks adopt a coiled coil structure with three core residues per α-helix. Three residue cores contribute a larger hydrophobic interface than two residues in the core (Deng et al., 2006)—a feature that would assist coiled coil formation and stability. [0295] In addition, when viewed collectively the positions b, c, e, f and g within the heptad are generally more hydrophobic, less polar and less charged than protein coiled coil regions previously characterised (see FIG. 7, and Tables 8 and 9). Therefore, although historically it was regarded that the helical content of the aculeate Hymenopteran silk was a consequence of a reduced glycine content and increased content of acidic residues (Rudall and Kenchington, 1971), we have discovered that it is not the glycine/acid residues that are responsible for the novel silk structure but rather the position of the alanine residues within the polypeptide chains.

TABLE 8

Average size and hydrophobicity at each heptad position of the orthologous hymenopteran silk proteins and of the green lacewing silk protein (MaIF1) showing that a, d, and e positions (core) are smaller and more hydrophobic than other positions. In some cases the b position (partially submerged) is also small and hydrophobic.

		Heptad position					
	a	b	c	d	e	f	g
		Amel	F1 orth	ologs			
Average residue side chain	0.36	0.20	0.20	0.30	0.26	-0.16	0.03
hydrophobicity Average residue side chain length	1.7	2.5	2.5	2.1	2.3	3.0	2.6
		Amel	F2 orth	ologs			
Average residue side chain	0.53	0.20	0.03	0.36	0.24	0.05	0.12
hydrophobicity Average residue side chain length	1.5	2.6	2.6	2.0	2.2	2.5	3.0
		Amel	F3 orth	ologs			
Average residue side chain	0.44	0.36	0.06	0.41	0.27	-0.10	0.00
hydrophobicity Average residue side chain length	1.9	2.3	2.4	2.1	2.3	2.8	2.8
		Amel	F4 orth	ologs			
Average residue side chain	0.46	0.17	-0.13	0.61	0.04	0.06	0.06
hydrophobicity Average residue side chain length	1.4	2.2	2.6	2.04	2.3	2.6	2.7
			MalF1				
Average residue side chain	-0.05	0.14	-0.61	0.27	0.59	0.23	-0.22
hydrophobicity Average residue side chain length	2.1	1.7	2.5	1.4	1.5	1.7	3.5

#### Example 6

The Bee Silk Proteins are Likely to be Extensively Cross-Linked

[0296] The bee silk proteins all contain a high proportion of lysine (6.5%-16.3%). A comparison between the mea-

sured amino acid composition of bee silk and the sequences of the identified silk proteins reveals a substantial mismatch in the number of lysine residues, with much less lysine detected in the silk than expected (FIGS. 2 and 3). This suggests that lysine residues in the silk have been modified, so are not being identified by standard amino acid analysis. Lysine is known to form a variety of cross-links: either enzymatic cross links catalysed by lysyl oxidase or nonenzymatic cross links generated from glycated lysine residues (Reiser et al., 1992). The under-representation of lysine in the honeybee and bumblebee silk amino acid analysis is consistent with the presence of lysine cross-linking

TABLE 9

Number of residues in each class of amino acids at various heptad positions in coiled coil regions of silk proteins.

Nonpolar	Polar	Charged	Small	Medium	Large	Heptad position
			Xenos	pira4		
25	2	2	26	2	1	a
16	7	6	19	10	ō	b
15	6	8	18	11	0	c
24	3	2	21	8	0	d
14	10	5	21	7	1	e
16	4	9	15	14	0	f
15	4	10	15	10	4	g
			Xenos	pira3		
20	8	2	24	5	1	a
13	13	4	15	15	0	b
17	6	7	20	8	2	c
20	5	5	19	11	0	d
11	13	6	18	12	0	e
10	9	11	13	15	2 5	f
13	7	10	16	9	5	g
			Xenos	pira2		
23	4	1	25	2	1	
23 15	7	6	23 14	12	2	a b
13	7	8	15	11	2	c
20	4	4	19	9	0	d
15	7	6	17	10	1	e
13	7	8	16	11	1	f
14	7	7	10	17	1	g
			Xenos			
20	4	3	18	9	0	
10	4	13	11	15	1	a b
13	4	10	13	12	2	c
20	5	2	22	5	0	d
15	6	6	19	6	2	e
10	9	8	18	6	3	f
18	4	5	17	10	0	g

[0297] Covalently cross-linked proteins subjected to SDS polyacrylamide gel electrophoresis (PAGE) are expected to migrate according to the molecular weight of the cross-linked complex. We subjected late last instar honeybee labial gland proteins to SDS PAGE and measured the migration of the silk proteins in relation to standard protein markers. Bands were observed corresponding to monomers of each of the identified silk proteins, however higher molecular weight bands containing these proteins were also present, as expected in a cross-linked system (FIG. 8).

[0298] As described above, the honeybee labial gland contains a mixture of organised and disorganised silk proteins. The cross-linked proteins observed probably correspond to the protein population of the anterior region of the gland, where the silk is prepared for extrusion. It is reason-

able to assume that extracellular honeybee silk contains a substantially higher proportion of cross-linked proteins than is observed in a heterogenous mixture of all stages of salivary gland silk proteins. The bonds are unlikely to be cysteine cross-links, as the silk was unaffected by reductive treatment, and the identified silk proteins contain few or no cysteine residues.

# Example 7

# The Euaculeatan Silk Proteins Differ Significantly from the Other Silk Proteins

[0299] The euaculeatan silk is significantly different from other described silk genes in relation to amino acid composition (Table 10), molecular weight of the proteins involved, secondary structure and physical properties (Tables 11 and 12). The lepidopteran silks are primarily composed of the small amino acid residues alanine, serine and glycine (for example the silk of Bombyx mori, Table 10) and are dominated by extended beta sheet secondary structure. The Cotesia glomerata silk protein is high in asparagine and serine—the abundance of the latter residue being characteristic of Lepidopteran silk sericins (glues) (Table 10). Modelling of the Cotesia glomerata silk protein does not identify helices or coiled coils in the secondary structure. In contrast, the bee, ant and lacewing silks are high in alanine (Table 10) and are comprised of a high level of helical secondary structure that forms coiled coils.

TABLE 10

Amino acid composition of silk from various Insects with most abundant residues shown in boldface.									
	Honeybee	Euaculeatan silk	<i>Mallada</i> silk	Cotesia glomerata	Bombyx mori				
Alanine	22.6	27.5	26.9	12.5	29.3				
Glutamic acid +	16.1	13.9	7.4	0.6	0.9				
Glutamine Aspartic acid +	13.2	8.6	15.0	37.6 (Asn 33.7)	1.2				
Asparagine Serine	10.4	11.5	8.5	37.1	11.3				
Leucine	9.0	7.2	5.9	0.4	0.4				
Valine	6.6	4.8	4.1	0.3	2.1				
Glycine	5.7	6.6	11.2	5.5	46.0				

TABLE 10-continued

Amino acid composition	of silk from	various Insects
with most abundant re-	sidues showi	in boldface.

	Honeybee	Euaculeatan silk	<i>Mallada</i> silk	Cotesia glomerata	Bombyx mori
Isoleucine	5.6	4.0	3.9	0.4	0.6
Threonine	5.1	4.9	5.3	0.5	0.8
Lysine	3.7	3.7	3.2	0.1	0.3
Phenyl-	2.0	1.0	0.5	0.5	0.6
alanine					
Tyrosine	0	0.9	0.5	3.1	5.3
Proline	0	0	0	0.7	0.4
Histidine	0	0.5	0.5	0.4	0.2
Arginine	0	3.3	5.4	0.2	0.4
Methionine	0	1.0	1.6	0	0.1
Tryptophan	0	Not	Not	Not	0.2
Cysteine	0	reported 0.4	reported 0.3	reported Not reported	0.1

TABLE 11

	Differe	ences between	insect silks.	
	Ant and bee silk	<i>Mallada</i> silk	Cotesia sp.	Lepidoptera For example Bombyx mori
Most abundant amino acids	Ala	Ala	Ser, Asn	Gly, Ala
Size of fibroin proteins	25-35 kDa	57 KDa	Approx 500 KDa	>100 KDa
Secondary structure	Coiled coil	Coiled coil	Most likely beta sheets. Secondary structure prediction programs PROFsec and MARCOIL do not recognise any helical structure or coiled coil regions.	beta-pleated sheets loosely associated with beta- sheets, beta- spirals, alpha helices and amorphous regions

TABLE 12

		Sol	ubility of	insect silk	s.			
		nd bee	Malla	da silk_	Cotes	aia sp.	Bomby	x mori
Solvent	20° C.	95° C.	20° C.	95° C.	20° C.	95° C.	20° C.	95° C.
LiBr 54%	_	_	_	_	_	part	_	1
LiSCN saturated	_	_	_	_	_	part	_	1
8M urea	_	_	_	_	_	_	_	part
6M guanidine HCl	_	_	_	_	_	_	_	part
1M NaOH	_	part	?	?	_	part	part	1
6M HCl	_	part	part	1	_	part	_	1
3M HCl/50% propanoic acid	_	part	?	?	_	part	part	1

[0300] Cladistic analysis of the coiled coil regions of the silk proteins of the four Hymenopteran species (FIG. 9) suggests that the genes evolved in a common ancestor that predates the divergence of the Euaculeata from the parasitic wasps. The sequences of the silk have diverged extensively and we were only able to align the 210 amino acids that comprise the coiled coil region of each protein. The amino acid sequence identity between the coiled coil regions of each of the silk proteins provided herein is shown in Table 13 and DNA identity in the corresponding region is shown in Table 14. Whilst the proteins have similar amino acid contents (especially high levels of alanine) and tertiary structure, the primary amino acid sequence identity is very low. In fact, the gene encoding the *Mallada* silk protein has evolved independently and as such the silk protein sequence

cannot be aligned to the Hymenopteran sequences. This indicates that considerable variety in the identity of the amino acids can occur, whilst not affecting the biological function of the proteins.

[0301] The cladistic analysis predicts that silk of euaculeatan wasps is comprised of related proteins to the silk of ants and bees and that although these proteins will have similar composition and architecture to the proteins described here, they will have highly diverged primary sequence.

[0302] The amino acid sequences of the silk proteins provided herein (FIG. 10) were subjected to comparisons with protein databases, however, no prior art proteins were identified with any reasonable level of sequence identity (for example, none greater than 30% identical over the length of the silk protein sequence).

TABLE 13

		Hone	ybee			Bumb	lebee			Bulld	og ant			Gree	n ant	
	F1	F2	F3	F4	F1	F2	F3	F4	F1	F2	F3	F4	F1	F2	F3	F4
beeF1	100															
beeF2	26.7	100														
beeF3	23.3	31.4	100													
eeF4	34.8	32.4	30.0	100												
BBF1	65.7	28.1	24.8	35.7	100											
BBF2	28.6	71.4	28.6	31.9	31.0	100										
BBF3	25.2	31.0	65.7	27.6	27.1	29.5	100									
BBF4	33.3	31.0	29.5	64.8	34.8	31.4	28.1	100								
BAF1	37.1	20.0	20.0	32.4	39.5	21.4	21.4	29.1	100							
BAF2	25.2	44.3	29.5	33.8	28.1	38.1	28.6	27.6	27.1	100						
BAF3	23.8	26.2	36.7	28.1	24.8	25.2	36.7	28.1	21.0	27.6	100					
BAF4	28.1	33.8	24.8	45.2	28.6	33.8	23.3	43.8	26.1	27.6	25.2	100				
GAF1	33.8	20.0	23.8	32.9	36.2	22.9	23.8	29.1	66.7	28.1	25.2	28.6	100			
GAF2	24.8	41.9	27.6	29.5	28.1	39.5	29.0	26.7	21.9	66.2	23.8	26.7	23.8	100		
GAF3	26.9	28.8	40.1	31.6	25.5	28.3	38.2	30.2	24.0	28.3	62.7	27.4	27.4	26.4	100	
GAF4	24.7	32.4	24.3	37.6	27.1	32.4	24.8	38.1	23.9	29.5	21.0	63.3	24.8	27.6	24.1	10

TABLE 14

Percent identity between nucleotide sequences encoding coiled coil region

		Hone	eybee			Bumb	lebee			Bulld	og ant			Gree	n ant	
	F1	F2	F3	F4	F1	F2	F3	F4	F1	F2	F3	F4	F1	F2	F3	F4
beeF1	100															
beeF2	39.4	100														
beeF3	37.0	40.2	100													
beeF4	45.1	44.8	41.0	100												
BBF1	68.9	40.9	37.5	45.2	100											
BBF2	42.5	72.9	42.5	44.9	42.2	100										
BBF3	40.6	40.0	67.6	40.5	38.4	41.0	100									
BBF4	45.4	41.0	41.7	66.0	45.9	43.6	40.0	100								
BAF1	45.7	35.1	35.9	41.1	47.9	36.5	36.0	38.7	100							
BAF2	38.1	49.8	41.4	44.6	38.7	47.3	40.0	41.0	40.6	100						
BAF3	33.3	36.7	45.4	40.3	36.3	36.8	46.2	39.4	36.0	40.5	100					
BAF4	39.5	43.3	41.4	46.8	43.0	47.6	39.8	49.4	42.5	41.7	40.3	100				
GAF1	45.6	35.1	37.3	42.4	47.6	38.5	37.8	41.4	68.9	41.7	36.7	43.0	100			
GAF2	38.5	47.8	38.4	43.2	38.1	46.5	41.4	40.0	37.5	69.7	38.9	40.6	39.4	100		
GAF3	39.0	40.1	46.1	41.8	37.7	39.3	46.1	40.0	37.7	41.7	65.1	41.2	40.0	41.7	100	
GAF4	38.9	42.4	38.1	44.9	38.9	43.8	38.4	44.3	37.3	42.7	36.7	67.8	38.2	40.3	37.7	100

[0303] The open reading frames encoding the silk proteins (provided on FIG. 11) were subjected to similar database searching as that described above. The only related molecules that were identified have been published as part of the honeybee genome project (www.ncbi.nlm.nih.gov/genome/guide/bee). The open reading frames had been predicted by the bee genome project, however, the function of the encoded proteins had not been suggested. Furthermore, there is no evidence that a polynucleotide comprising the open reading frame of the mRNA had ever been produced for any of these molecules.

[0304] The genes encoding Xenospira1, Xenospira2, Xenospira3 and Xenospira4 comprise an exon covering the entire single open reading frame, whereas the gene encoding Xenosin comprises at least one intron (see FIG. 12).

## Example 8

#### Expression of Silk Proteins in Transgenic Plants

[0305] A plant expression vector encoding a silk protein of the invention may consist of a recombinant nucleic acid molecule coding for said protein (for example a polynucleotide provided in any one of SEQ ID NO's: 11 to 21, 31 to 39, 48 to 55, 64 to 71, 74 or 75) placed downstream of the CaMV 35S promoter in a binary vector backbone containing a kanamycin-resistance gene (NptII).

[0306] For the polynucleotides comprising any one of SEQ ID NO's 11, 13, 15, 17, 19, 31, 33, 35, 37, 48, 50, 52, 54, 64, 66, 68, 70 or 74 the construct further may comprise a signal peptide encoding region such as *Arabidopsis thaliana* vacuolar basic chitinase signal peptide, which is placed in-frame and upstream of the sequence encoding the silk protein.

[0307] The construct carrying a silk protein encoding polypeptide is transformed separately into *Agrobacterium tumefaciens* by electroporation prior to transformation into *Arabidopsis thaliana*. The hypocotyl method of transformation can be used to transform *A. thaliana* which can be selected for survival on selective media comprising kanamycin media. After roots are formed on the regenerates they are transferred to soil to establish primary transgenic plants.

[0308] Verification of the transformation process can be achieved via PCR screening. Incorporation and expression of polynucleotide can be measured using PCR, Southern blot analysis and/or LC/MS of trypsin-digested expressed proteins.

[0309] Two or more different silk protein encoding constructs can be provided in the same vector, or numerous different vectors can be transformed into the plant each encoding a different protein.

[0310] As an experimental example of plant expression, a codon-optimised version of AmelF4 (Xenospira4) (SEQ ID NO:76) was cloned into pET14b (Novagen), generating pET14b-6×His:F4op, forming an in-frame translational fusion with a 6×histidine at the N-terminal of the protein. The sequence encoding the protein "6×Histidine:F4op" was cloned into pVEC8 (Wang et al., 1992) under the control of the CaMV 35S promoter and ocs polyadenylation regulatory apparatus, generating pVEC8-35S-6×His:F4op-ocs. pET14b-6×His:F4op was transformed into chemically-competent *E. coli* and pVEC8-35S-6×His:F4op was transformed into tobacco leaf discs by *Agrobacterium* mediated transformation. Proteins from antibiotic resistant *E. coli* (induced expression) and tobacco leaves were isolated and subjected

to western blot analysis using the Tetra-Histidine antibody (Qiagen, Karlsrule, Germany) for detection. The empty vectors pET14b and pVEC8-35S-ocs were used as negative controls in there respective host backgrounds. As shown in FIG. 13, these experiments resulted in the plant producing the Xenospira4 (AmelF4) protein.

#### Example 9

#### Fermentation and Purification of Silk Proteins

[0311] Expression constructs were constructed after the silk coding regions of honeybee genes AmelF1-F4 (Xenospira1 to 4 respectively) and lacewing MalF1 genes were amplified by PCR and cloned into pET14b expression vectors (Novagen, Madison, Wis.). The resultant expression plasmids were then electroporated into *E. coli* BL21 (DE3) Rosetta cells and grown overnight on LB agar containing ampicillin. A single colony was then used to inoculate LB broth containing ampicillin then grown at 37° C. overnight. Cells were harvested by centrifugation and lysed with detergent (Bugbuster, Novagen). Inclusion bodies were washed extensively and re-solubilised in 6M guanidinium.

**[0312]** This procedure yielded proteins mixtures with greater than 95% purity of the honeybee proteins and greater than 50% purity of the lacewing MalF1 protein. Yields of up to 50% of the wet weight of the *E. coli* cell pellet were regularly obtained, indicating that the proteins are easy to express in this manner.

[0313] The solubilised honeybee recombinant proteins were applied to a Talon resin column prepared according to manufactures directions. They were then eluted off the column in 100 mM Tris.HCL, 150 mM imidazole pH 8.

#### Example 10

#### Processing of Silk Proteins into Threads

[0314] The honeybee and lacewing silk proteins have been readily made into threads using a variety of methods (see FIG. 14) using the following procedure.

[0315] The anterior segment of the salivary gland from late final instar *Apis mellifera* was dissected under phosphate buffered saline and removed to a flat surface in a droplet of buffer. Forceps were used to grasp either end of the segment. One end was raised out of the droplet and away from the other at a steady rate. This enabled the drawing of a fine thread that rapidly solidified in air.

[0316] The honeybee and lacewing larval recombinant silk proteins formed threads or sheets after dehydration or concentration. For example, by dropping soluble protein into a butanol solution or by concentrating proteins on the Talon resin column.

[0317] Threads were also obtained after honeybee or lacewing recombinant silk proteins were mixed with an organic solvent (such as hexane) to concentrate them at the interface in the correct conformation, and then addition of a reagent to exclude them from the interface (such as butanol). The threads formed by this procedure had similar FT-IR spectra to the native silk indicating that they were comprised of the same coiled coil structure.

[0318] Silk proteins from other species described herein can also be processed by this procedure.

[0319] It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the invention as shown in the specific embodiments

without departing from the spirit or scope of the invention as broadly described. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

[0320] All publications discussed above are incorporated herein in their entirety.

[0321] Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is solely for the purpose of providing a context for the present invention. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this application.

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SEQUENCE LISTING

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Gln	Ala	Ala	Asn 260	Ala	Glu	Ala	Ala	Ala 265	Val	Ala	Gln	Ala	Glu 270	Thr	Leu
Leu	Val	Thr 275	Ala	Glu	Ala	Val	Ala 280	Ala	Ala	Glu	Ala	Glu 285	Val	Ala	Asn
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Arg	Glu	Asn 35	Gly	Ala	Pro	Val	Leu 40	Gly	Lys	Asn	Thr	Leu 45	Gln	Ser	Leu
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Val 65	ГЛа	Ala	Ser	Ala	Leu 70	Ala	Leu	Ala	Glu	Ala 75	Tyr	Leu	Arg	Ala	Ser 80
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Ala	Gln	Gln	Ala 100	Gln	Leu	Asn	Ala	Gln 105	Glu	Lys	Ser	Leu	Ala 110	Ala	Leu
ГÀа	Ala	Gln 115	Ser	Glu	Glu	Glu	Ala 120	Ala	Ser	Ala	Arg	Ala 125	Asn	Ala	Ala
Thr	Ala 130	Ala	Thr	Gln	Ser	Ala 135	Leu	Glu	Arg	Ala	Gln 140	Ala	Ser	Ser	Arg
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Asp	Ala	Glu	Arg 180	Thr	Lys	Trp	Ser	Ala 185	Asn	Ala	Ala	Leu	Glu 190	Val	Ser
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Ala	Asn 210	Ala	Ala	Ala	Lys	Lys 215	Ala	Ala	Ala	Ile	Ala 220	Ser	Asp	Ala	Asp
Gly 225	Ala	Glu	Arg	Ser	Ala 230	Ser	Thr	Glu	Ala	Gln 235	Ser	Ala	Ala	Tàs	Ile 240
Glu	Ser	Val	Ala	Ala 245	Ala	Glu	Gly	Ser	Ala 250	Asn	Ser	Ala	Ser	Glu 255	Asp

Ser	Arg	Ala	Ala 260	Gln	Leu	Glu	Ala	Ser 265	Thr	Ala	Ala	Arg	Ala 270	Asn	Val
Ala	Ala	Ala 275	Val	Gly	Asp	Gly	Ala 280	Ile	Ile	Gly	Leu	Gly 285	Glu	Glu	Ala
Gly	Ala 290	Ala	Ala	Gln	Leu	Leu 295	Ala	Gln	Ala	Lys	Ala 300	Leu	Ala	Glu	Val
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Ile	Ser	35 Lys	Asn	Leu	Glu	Val	Asp 40	Leu	Leu	Lys	Asn	Val 45	Asp	Thr	Ser
Ala	Lys 50	Arg	Arg	Glu	Asn	Gly 55	Ala	Pro	Val	Leu	Gly 60	rys	Asn	Thr	Leu
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Ala	Ala	Val	Val	Lys 85	Ala	Ser	Ala	Leu	Ala 90	Leu	Ala	Glu	Ala	Tyr 95	Leu
Arg	Ala	Ser	Ala 100	Leu	Ser	Ala	Ala	Ala 105	Ser	Ala	Lys	Ala	Ala 110	Ala	Ala
Leu	Lys	Asn 115	Ala	Gln	Gln	Ala	Gln 120	Leu	Asn	Ala	Gln	Glu 125	Lys	Ser	Leu
Ala	Ala 130	Leu	Lys	Ala	Gln	Ser 135	Glu	Glu	Glu	Ala	Ala 140	Ser	Ala	Arg	Ala
Asn 145	Ala	Ala	Thr	Ala	Ala 150	Thr	Gln	Ser	Ala	Leu 155	Glu	Arg	Ala	Gln	Ala 160
Ser	Ser	Arg	Leu	Ala 165	Thr	Val	Ala	Gln	Asn 170	Val	Ala	Ser	Asp	Leu 175	Gln
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Gln	Leu	Gln 195	Asp	Ala	Glu	Arg	Thr 200	Lys	Trp	Ser	Ala	Asn 205	Ala	Ala	Leu
Glu	Val 210	Ser	Ala	Ala	Ala	Ala 215	Ala	Ala	Glu	Thr	Lys 220	Thr	Thr	Ala	Ser
Ser 225	Glu	Ala	Ala	Asn	Ala 230	Ala	Ala	Lys	Lys	Ala 235	Ala	Ala	Ile	Ala	Ser 240
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Ala	Lys	Ile	Glu 260	Ser	Val	Ala	Ala	Ala 265	Glu	Gly	Ser	Ala	Asn 270	Ser	Ala
Ser	Glu	Asp 275	Ser	Arg	Ala	Ala	Gln 280	Leu	Glu	Ala	Ser	Thr 285	Ala	Ala	Arg
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340

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Ala	Ser	Lуs 35	Ser	Lys	Ser	Glu	Arg 40	Leu	Lys	Ile	Arg	Glu 45	Glu	Lys	Arg
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Lys 65	Ile	Thr	Lys	Leu	Ser 70	Ser	Trp	Leu	Lys	Glu 75	Glu	Lys	Asp	Ile	Ser 80
Pro	Leu	Leu	Glu	Glu 85	Lys	Asn	Gly	Lys	Gly 90	Leu	Leu	Gly	Leu	Glu 95	Asp
Val	Thr	Asp	Glu 100	Leu	Asn	Ile	Ala	Leu 105	Lys	Ser	Leu	Lys	Glu 110	Gly	Lys
Lys	Phe	Asp 115	Thr	Trp	Lys	Phe	Glu 120	Lys	Gly	Ser	Glu	Asp 125	Val	Arg	Ser
Leu	Glu 130	Glu	Leu	Asp	Thr	Ser 135	Val	Val	Glu	Leu	Leu 140	ГÀа	Leu	Ile	Lys
Glu 145	Gly	Lys	Thr	Asp	His 150	Gly	Ala	Ile	Asp	Leu 155	Glu	ГÀа	Asn	Gly	Lys 160
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Trp	Asn	Lys 195	Glu	Ser	Gly	Trp	Lys 200	ГЛа	Asn	Leu	Asn	Asp 205	Leu	Asp	Trp
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Val	Glu	Arg 275	Asn	Leu	Asp	Leu	Lys 280	Leu	Phe	Thr	Ser	Ser 285	Val	Ser	ГЛа
Val	Thr 290	Glu	Leu	Leu	Asn	Lув 295	Gly	Ile	Asp	Ile	Gln 300	Thr	Ile	Leu	Asn
Ala 305	Lys	Asn	Gly	Asp	Glu 310	Phe	Asp	Leu	Ser	Gly 315	Lys	Glu	Leu	Lys	Asn 320
Val	Lys	Gly	Ile	Phe 325	Gly	Leu	Ile	Gly	Ser 330	Leu	Lys	Arg	Ser	Leu 335	Gly
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Leu

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Glu	Glu 50	Arg	Ala	Ser	Lys	Ser 55	Lys	Ser	Glu	Arg	Leu 60	Lys	Ile	Arg	Glu
Glu 65	ГЛа	Arg	Glu	Glu	Glu 70	Glu	ГЛа	Ser	Lys	Ser 75	Leu	Asn	Leu	Val	Val 80
Val	Arg	Glu	Lys	Ile 85	Thr	Lys	Leu	Ser	Ser 90	Trp	Leu	ГÀв	Glu	Glu 95	Lys
Asp	Ile	Ser	Pro 100	Leu	Leu	Glu	Glu	Lys 105	Asn	Gly	Lys	Gly	Leu 110	Leu	Gly
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Leu	Ile	Lys	Glu	Gly 165	rys	Thr	Asp	His	Gly 170	Ala	Ile	Asp	Leu	Glu 175	Lys
Asn	Gly	Lys	Val 180	Leu	Val	Asp	Leu	Glu 185	ГÀв	Ile	Ser	Glu	Asn 190	Ile	Leu
Glu	Thr	Сув 195	Gly	Ser	Gln	Lys	Lys 200	Thr	Val	Glu	Val	Val 205	Asp	Asp	Lys
Asp	Lys 210	Lys	Trp	Asn	Lys	Glu 215	Ser	Gly	Trp	Lys	Lys 220	Asn	Leu	Asn	Asp
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gccgaagctg tagtggcact aacaaacgcc gaagtcgccg tgaaccaggc tagaaacgca	720
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gctgaagcag ccgctgtagc gcaagccgaa actctcttgg ttacggcaga agctgtcgca	840
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ggcaagaaca cacttcaatc cctggagaag atcaagacgt cggcgagcgt gaatgccaaa	180
gcagcagccg tggtgaaagc gtccgctctg gctcttgcag aggcctattt gcgagcgtcc	240
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gettetgete gtgcaaacge agcaaccgee gegacacagt eggcaetgga aegegeteaa	420
gcctcctcca ggttagcaac ggtcgcccaa aacgtagcca gcgacttgca gaaacggacc	480
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acgaaatgga gtgccaacgc tgccttagaa gtctccgccg ctgcagctgc cgcagaaacc	600
aagaccactg ceteetegga ggeegecaac geegeegeca aaaaggegge egegataget	660
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aagaacacac ttcaatccct ggagaagatc aagacgtcgg cgagcgtgaa tgccaaagca	240
gcagccgtgg tgaaagcgtc cgctctggct cttgcagagg cctatttgcg agcgtccgca	300
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ttaaacgccc aggaaaagtc tttggccgcg ttgaaagctc agtccgagga agaggcagct	420
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accaaggeeg eggetgaage egetgeeace eteagacaat tacaggaege ggaaegaaeg	600
aaatggagtg ccaacgctgc cttagaagtc teegeegetg cagetgeege agaaaccaag	660
accactgcct cctcggaggc cgccaacgcc gccgccaaaa aggcggccgc gatagcttct	720
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ggaagaagag tgggaactgg agcatccgag gtggcatcta gcagcggtga agccatcgcg	180
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gctggcccgt tggcaggtga gatgaaacca ccgcactgga aatgggaacg gattcctgtg	900
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gtggaagteg ttgeteeege taaggatgaa ettaaattaa egagegagee tatetttgga	180
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agtettggag cagggcagte ageggeagag teteaggeet tggeegeete geaateeaaa

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	agcttggcga	ccgaagaagc	ggcggaagag	gccgaggcgg	ccgtggctga	cgccaaggct	480				
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	caggccaaga	cagcagccgc	cgccaaagca	gcggaaatcg	cccttaaggt	cgctgagata	660				
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	cttttgaata	agaatcaaat	tgagttatta	attcctttaa	tcagtgagat	aaaaaagaaa	780				
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780

840

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Ala	Ala 50	Ala	Ala	Ala	Ala	Ala 55	Arg	Ala	Ser	Ala	Asp 60	Gln	Ser	Ala	Ser	
Leu 65	Ala	Gln	Gln	Ser	Ala 70	Ser	Leu	Gln	Ser	Lys 75	Ala	Ala	Ala	Arg	Ala 80	
Lys	Ser	Ala	Glu	Glu 85	Ser	Ala	Ala	Ala	Thr 90	Ala	ГÀа	Ala	Glu	Leu 95	Gln	
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Glu 145	Ala	Lys	Leu	Lys	Ala 150	Ala	Ala	Ala	Ala	Ser 155	Ala	Ala	Ala	Ala	Ala 160	
Ser	Ala	Ala	Ala	Glu 165	Ala	Ala	Leu	Lys	Ala 170	Glu	Arg	Ile	Ala	Glu 175	Glu	

Ala Ile Ala Lys Ala Ala Ala Ala Lys Ala Ala Ala Arg Ala Ala Ala 180 185 190

Ala Ala Leu Asn Ser Ala Lys Glu Ala Ala Thr Ser Ser Ala Arg Ser 195  $\phantom{\bigg|}200\phantom{\bigg|}\phantom{\bigg|}\phantom{\bigg|}\phantom{\bigg|}205\phantom{\bigg|}\phantom{\bigg|}\phantom{\bigg|}\phantom{\bigg|}$ 

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Leu 225	Asp	Lys	Lys	Ser	Arg 230	Glu	Val	Ala	Ala	Ser 235	Ala	Ser	Ala	Lys	Ala 240
Arg	Ala	Ala	Ala	Ala 245	Ala	Ser	Ser	Arg	Asn 250	Ala	Glu	Thr	Ala	Val 255	Ile
Gly	Ala	Asn	Ile 260	Asn	Val	Ala	Lys	Glu 265	Val	Leu	Ala	Ile	Pro 270	Ile	Glu
Pro	Lys	Lys 275	Leu	Pro	Glu	Pro	Glu 280	Leu	Ala	Leu	Lys	Glu 285	Glu	Asn	Val
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Ala	Ser	Ala 35	Thr	Ala	Ser	Thr	Ala 40	Val	Thr	Ala	Arg	Ser 45	Gly	Leu	Arg
Ala	Gly 50	Gln	Val	Ala	Val	Ala 55	Ser	Gln	Lys	Asp	Ala 60	Thr	Leu	Gln	Ala
Asp 65	Ala	Ser	Ala	Ala	Ala 70	Ala	Ala	Ala	Ala	Arg 75	Ala	Ser	Ala	Asp	Gln 80
Ser	Ala	Ser	Leu	Ala 85	Gln	Gln	Ser	Ala	Ser 90	Leu	Gln	Ser	Lys	Ala 95	Ala
Ala	Arg	Ala	Lys 100	Ser	Ala	Glu	Glu	Ser 105	Ala	Ala	Ala	Thr	Ala 110	Lys	Ala
Glu	Leu	Gln 115	Ala	Glu	Ser	Ile	Ala 120	Ala	Ser	Ala	Ser	Ser 125	Asn	Ala	Arg
Glu	Ala 130	Ala	Ala	Ser	Ala	Lys 135	Ala	Ser	Ala	Ser	Ala 140	Met	Ser	Ser	Ala
Ala 145	Val	Gln	Ala	ГÀа	Leu 150	Ala	Glu	Lys	Thr	Ala 155	Lys	Asn	Gln	Ala	Leu 160
Ala	Ser	Glu	Glu	Ala 165	rys	Leu	Lys	Ala	Ala 170	Ala	Ala	Ala	Ser	Ala 175	Ala
Ala	Ala	Ala	Ser 180	Ala	Ala	Ala	Glu	Ala 185	Ala	Leu	Lys	Ala	Glu 190	Arg	Ile
Ala	Glu	Glu 195	Ala	Ile	Ala	ГЛа	Ala 200	Ala	Ala	Ala	ГЛа	Ala 205	Ala	Ala	Arg
Ala	Ala 210	Ala	Ala	Ala	Leu	Asn 215	Ser	Ala	Lys	Glu	Ala 220	Ala	Thr	Ser	Ser
Ala 225	Arg	Ser	Ala	Ala	Glu 230	Ala	Glu	Ala	Lys	Ser 235	Glu	Val	Ala	Ile	Leu 240
Ile	Ser	Glu	Leu	Asp 245	Lys	Lys	Ser	Arg	Glu 250	Val	Ala	Ala	Ser	Ala 255	Ser

Ala Lys Ala Arg Ala Ala Ala Ala Ser Ser Arg Asn Ala Glu Thr 260 265 270
Ala Val Ile Gly Ala Asn Ile Asn Val Ala Lys Glu Val Leu Ala Ile 275 280 285
Pro Ile Glu Pro Lys Lys Leu Pro Glu Pro Glu Leu Ala Leu Lys Glu 290 295 300
Glu Asn Val Ala Val Ala Ser Ser Glu Ser Glu Val Lys Val Glu Thr 305 310 315 320
Ser Ser Glu Ala Trp Ser Ile 325
<210> SEQ ID NO 24 <211> LENGTH: 293 <212> TYPE: PRT
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His Val Val Lys Arg Asp Lys Glu Leu Lys Ala Pro Ala Leu Pro Glu 1 5 10 15
Leu Leu Gly Asp Gly Ser Asp Thr Leu Gly Ala Ser Met Glu Asn Gly 20 25 30
Ile Lys Val Ala Arg Ala Ser Gln Asn Val Gly Leu Arg Thr Glu Leu 35 40 45
Asn Ala Ala Ala Arg Ala Ala Ala Ala Ala Ala Thr Lys Gln Ala Lys 50 55 60
Asp Thr Glu Ala Ala Glu Ala Gly Ala Ala Ala Ala Ile Ala Ile Ala 65 70 75 80
Ile Ala Lys Arg Glu Glu Ala Ile Lys Ala Ser Glu Leu Ala Ser Lys 85 90 95
Leu Leu Thr Ala Ala Ala Gly Ser Ser Glu Ala Ala Val Ser Ala Thr 100 105 110
Val Arg Ala Ala Gln Leu Thr Ala Ala Ala Ser Ala Ala Ala Lys Ala 115 120 125
Ser Ala Ser Ala Ser Glu Ala Ser Ala Glu Ala Gln Val Arg Ala Asn 130 135 140
Ala Glu Ala Asn Ile Ala Lys Lys Ala Ser Ala Ala Glu Ala Lys Ala 145 150 150 155 160
Ala Ala Glu Ala Gln Val Lys Ala Glu Leu Ala Lys Lys Ala Ala Ala 165 170 175
Gly Phe Leu Ala Lys Ala Arg Leu Ala Ala Ser Ala Glu Ser Glu Ala 180 185 190
Thr Lys Leu Ala Ala Glu Ala Glu Val Ala Leu Ala Lys Ala Arg Val 195 200 205
Ala Val Asp Gln Ser Gln Ser Ala Gln Ala Thr Ala Thr Ala Gln Ala 210 215 220
Ala Thr Ala Val Gln Leu Gln Ser Gln Ala Ala Asn Ala Glu Ala Ser 225 230 235 240
Ala Val Ala Gln Ala Glu Thr Leu Leu Val Thr Ala Glu Ala Val Ser 245 250 255
Ala Ala Glu Ala Glu Ala Ala Thr Lys Ala Thr Ser Trp Gly Glu Glu 260 265 270
Cys His Gln Arg Glu Lys Val Thr Phe Ser Glu Asp Arg Leu Asn Glu

_		275					280					285			
Arg	Gln 290	Asp	Asn	Trp											
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			ISM:		ous t	erre	estr:	ĹS							
			Pro		Ile	Leu	Val	Thr	Ser 10	Leu	Leu	Val	Trp	Gly 15	Gly
Leu	Ala	Glu	Gly 20	His	Val	Val	Lys	Arg 25	Asp	Lys	Glu	Leu	Lys 30	Ala	Pro
Ala	Leu	Pro 35	Glu	Leu	Leu	Gly	Asp 40	Gly	Ser	Asp	Thr	Leu 45	Gly	Ala	Ser
Met	Glu 50	Asn	Gly	Ile	Lys	Val 55	Ala	Arg	Ala	Ser	Gln 60	Asn	Val	Gly	Leu
Arg 65	Thr	Glu	Leu	Asn	Ala 70	Ala	Ala	Arg	Ala	Ala 75	Ala	Ala	Ala	Ala	Thr 80
rys	Gln	Ala	Lys	Asp 85	Thr	Glu	Ala	Ala	Glu 90	Ala	Gly	Ala	Ala	Ala 95	Ala
Ile	Ala	Ile	Ala 100	Ile	Ala	Lys	Arg	Glu 105	Glu	Ala	Ile	ГÀа	Ala 110	Ser	Glu
Leu	Ala	Ser 115	Lys	Leu	Leu	Thr	Ala 120	Ala	Ala	Gly	Ser	Ser 125	Glu	Ala	Ala
Val	Ser 130	Ala	Thr	Val	Arg	Ala 135	Ala	Gln	Leu	Thr	Ala 140	Ala	Ala	Ser	Ala
Ala 145	Ala	Lys	Ala	Ser	Ala 150	Ser	Ala	Ser	Glu	Ala 155	Ser	Ala	Glu	Ala	Gln 160
Val	Arg	Ala	Asn	Ala 165	Glu	Ala	Asn	Ile	Ala 170	Lys	ГАз	Ala	Ser	Ala 175	Ala
Glu	Ala	ГЛа	Ala 180	Ala	Ala	Glu	Ala	Gln 185	Val	ГЛа	Ala	Glu	Leu 190	Ala	Lys
ГÀа	Ala	Ala 195	Ala	Gly	Phe	Leu	Ala 200	Lys	Ala	Arg	Leu	Ala 205	Ala	Ser	Ala
Glu	Ser 210	Glu	Ala	Thr	ràa	Leu 215	Ala	Ala	Glu	Ala	Glu 220	Val	Ala	Leu	Ala
Lys 225	Ala	Arg	Val	Ala	Val 230	Asp	Gln	Ser	Gln	Ser 235	Ala	Gln	Ala	Thr	Ala 240
Thr	Ala	Gln	Ala	Ala 245	Thr	Ala	Val	Gln	Leu 250	Gln	Ser	Gln	Ala	Ala 255	Asn
Ala	Glu	Ala	Ser 260	Ala	Val	Ala	Gln	Ala 265	Glu	Thr	Leu	Leu	Val 270	Thr	Ala
Glu	Ala	Val 275	Ser	Ala	Ala	Glu	Ala 280	Glu	Ala	Ala	Thr	Lys 285	Ala	Thr	Ser
Trp	Gly 290	Glu	Glu	Cys	His	Gln 295	Arg	Glu	Lys	Val	Thr 300	Phe	Ser	Glu	Asp
Arg 305	Leu	Asn	Glu	Arg	Gln 310	Asp	Asn	Trp							
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<210> SEQ ID NO 26 <211> LENGTH: 313

<212> TYPE: PRT <213> ORGANISM: Bombus terrestris <400> SEQUENCE: 26 Gly Ser Val Glu Leu Gly Ala Pro Lys Gln Glu Ser Val Leu Val Glu Gln Leu Leu Lys Asn Val Glu Thr Ser Ala Lys Arg Lys Glu Asn Gly Ala Pro Lys Leu Gly Glu Ser Thr Ala Ala Ala Leu Ala Ser Thr Lys Ala Thr Ala Ala Ala Glu Ala Lys Ala Ser Ala Lys Val Lys Ala Ser Ala Leu Ala Leu Ala Glu Ala Phe Leu Arg Ala Ser Ala Ala Phe 65 70 75 80 Ala Ala Ala Ser Ala Lys Ala Ala Ala Val Lys Glu Ala Thr Gln Ala Gln Leu Leu Ala Gln Glu Lys Ala Leu Ile Ala Leu Lys Thr Gln 105 Ser Glu Gln Gln Ala Ala Ser Ala Arg Ala Asp Ala Ala Ala Ala Ala 120 Ala Val Ser Ala Leu Glu Arg Ala Gln Ala Ser Ser Arg Ala Ala Thr Thr Ala Gln Asp Ile Ser Ser Asp Leu Glu Lys Arg Val Ala Thr Ser 155 Ala Ala Ala Glu Ala Gly Ala Thr Leu Arg Ala Glu Gln Ser Ala Ala Gln Ser Lys Trp Ser Ala Ala Leu Ala Ala Gln Thr Ala Ala Ala Ala 185 Ala Ala Ile Glu Ala Lys Ala Thr Ala Ser Ser Glu Ser Thr Ala Ala Ala Thr Ser Lys Ala Ala Val Leu Thr Ala Asp Thr Ser Ser Ala Glu 215 Ala Ala Ala Ala Glu Ala Gln Ser Ala Ser Arg Ile Ala Gly Thr Ala Ala Thr Glu Gly Ser Ala Asn Trp Ala Ser Glu Asn Ser Arg Thr Ala Gln Leu Glu Ala Ser Ala Ser Ala Lys Ala Thr Ala Ala Ala Ala Val Gly Asp Gly Ala Ile Ile Gly Leu Ala Arg Asp Ala Ser Ala Ala Ala Gln Ala Ala Glu Val Lys Ala Leu Ala Glu Ala Ser Ala Ser 295 Leu Gly Ala Ser Glu Lys Asp Lys Lys 310 <210> SEQ ID NO 27 <211> LENGTH: 332 <212> TYPE: PRT <213> ORGANISM: Bombus terrestris <400> SEQUENCE: 27 Met Gln Ile Pro Ala Ile Phe Val Thr Cys Leu Leu Thr Trp Gly Leu

Val His Ala Gly Ser Val Glu Leu Gly Ala Pro Lys Gln Glu Ser Val Leu Val Glu Gln Leu Leu Lys Asn Val Glu Thr Ser Ala Lys Arg Lys Glu Asn Gly Ala Pro Lys Leu Gly Glu Ser Thr Ala Ala Ala Leu Ala Ser Thr Lys Ala Thr Ala Ala Ala Glu Ala Lys Ala Ser Ala Lys Val Lys Ala Ser Ala Leu Ala Leu Ala Glu Ala Phe Leu Arg Ala Ser Ala Ala Phe Ala Ala Ala Ser Ala Lys Ala Ala Ala Val Lys Glu Ala Thr Gln Ala Gln Leu Leu Ala Gln Glu Lys Ala Leu Ile Ala Leu Lys Thr Gln Ser Glu Gln Gln Ala Ala Ser Ala Arg Ala Asp Ala Ala Ala Ala Ala Val Ser Ala Leu Glu Arg Ala Gln Ala Ser Ser Arg Ala Ala Thr Thr Ala Gln Asp Ile Ser Ser Asp Leu Glu Lys Arg Val 170 Ala Thr Ser Ala Ala Ala Glu Ala Gly Ala Thr Leu Arg Ala Glu Gln 180 185 Ser Ala Ala Gln Ser Lys Trp Ser Ala Ala Leu Ala Ala Gln Thr Ala Ala Ala Ala Ala Ile Glu Ala Lys Ala Thr Ala Ser Ser Glu Ser 215 Thr Ala Ala Ala Thr Ser Lys Ala Ala Val Leu Thr Ala Asp Thr Ser 230 Ser Ala Glu Ala Ala Ala Ala Glu Ala Gln Ser Ala Ser Arg Ile Ala Gly Thr Ala Ala Thr Glu Gly Ser Ala Asn Trp Ala Ser Glu Asn Ser Arg Thr Ala Gln Leu Glu Ala Ser Ala Ser Ala Lys Ala Thr Ala 280 Ala Ala Ala Val Gly Asp Gly Ala Ile Ile Gly Leu Ala Arg Asp Ala Ser Ala Ala Ala Gln Ala Ala Glu Val Lys Ala Leu Ala Glu Ala Ser Ala Ser Leu Gly Ala Ser Glu Lys Asp Lys <210> SEQ ID NO 28 <211> LENGTH: 338 <212> TYPE: PRT <213> ORGANISM: Bombus terrestris <400> SEQUENCE: 28 Gly Lys Pro Leu Ile Ala Asn Ala Gln Ile Gly Lys Val Lys Thr Glu Thr Ser Ser Ser Glu Ile Glu Thr Leu Val Ser Gly Ser Gln Thr 25 Leu Val Ala Gly Ser Glu Thr Leu Ala Ser Glu Ser Glu Ala Leu Ala 40

Ser Lys Ser Glu Ala Leu Thr Ser Glu Ala Glu Ile Ala Ser Val Thr Thr Lys Asp Glu Leu Ile Leu Lys Gly Glu Ala Ile Thr Gly Lys Lys Leu Gly Thr Gly Ala Ser Glu Val Ala Ala Ala Ser Gly Glu Ala Ile Ala Thr Thr Leu Gly Ala Gly Gln Ala Ala Ala Glu Ala Gln Ala Ala Ala Ala Ala Gln Ala Lys Ser Ala Ala Ala Ala Ala Asn Ala Gly Glu Ser Ser Asn Ser Ala Ala Ala Leu Val Ala Ala Ala Ala Ala Ala Gln Gly Lys Ala Ala Ala Ala Ala Ala Ala Thr Lys Ala Ser Leu 150 155 Glu Ala Ala Asp Ala Ala Glu Glu Ala Glu Ser Ala Val Ala Leu Ala 165 170 Arg Ala Ala Ser Ala Lys Ala Glu Ala Leu Ala Ser Thr Ala Ala Ala 185 Ala Asn Thr Arg Ala Ala Leu Gln Ala Glu Lys Ser Asn Glu Leu Ala 200 Gln Ala Glu Ala Ala Ala Ala Glu Ala Gln Ala Lys Ala Ala Ala 215 Ala Ala Lys Ala Thr Gln Leu Ala Leu Lys Val Ala Glu Thr Ala Val 230 Lys Thr Glu Ala Asp Ala Ala Ala Ala Val Ala Ala Ala Lys Ala Arg Ala Val Ala Asp Ala Ala Ala Ser Arg Ala Thr Ala Val Asn Ala 265 Ile Ala Glu Ala Glu Glu Arg Asp Ser Ala Gln Ala Glu Asn Thr Ala Gly Val Ala Gln Ala Ala Leu Ala Ala Ala Glu Ala Gln Asp Ser Cys 295 Ile Gly Ala Ala Ala Thr Pro Arg His Ser Ser Ser Tyr Ala Trp Trp Lys Leu Arg Ile Thr Ser Leu Ile Val Ile Leu Ser Pro Arg Asn Arg Arg Thr <210> SEQ ID NO 29 <211> LENGTH: 357 <212> TYPE: PRT <213 > ORGANISM: Bombus terrestris <400> SEOUENCE: 29 Met Lys Ile Pro Ser Ile Leu Ala Val Ser Leu Leu Val Trp Gly Leu 10 Ala Ser Ala Gly Lys Pro Leu Ile Ala Asn Ala Gln Ile Gly Lys Val 25 Lys Thr Glu Thr Ser Ser Ser Glu Ile Glu Thr Leu Val Ser Gly 40 Ser Gln Thr Leu Val Ala Gly Ser Glu Thr Leu Ala Ser Glu Ser Glu 55

Ser Val Thr Thr Lys Asp Glu Leu Ile Leu Lys Gly Glu Ala Ile Thr Gly Lys Lys Leu Gly Thr Gly Ala Ser Glu Val Ala Ala Ala Ser Gly Glu Ala Ile Ala Thr Thr Leu Gly Ala Gly Gln Ala Ala Ala Glu Ala Gln Ala Ala Ala Ala Gln Ala Lys Ser Ala Ala Ala Ala Ala Ala Asn Ala Gly Glu Ser Ser Asn Ser Ala Ala Ala Leu Val Ala Ala Ala Ala Ala Ala Gln Gly Lys Ala Ala Ala Ala Ala Ala Ala Thr Lys 170 Ala Ser Leu Glu Ala Ala Asp Ala Ala Glu Glu Ala Glu Ser Ala Val 180 185 Ala Leu Ala Arg Ala Ala Ser Ala Lys Ala Glu Ala Leu Ala Ser Thr 200 Ala Ala Ala Asn Thr Arg Ala Ala Leu Gln Ala Glu Lys Ser Asn 215 Glu Leu Ala Gln Ala Glu Ala Ala Ala Ala Glu Ala Gln Ala Lys 235 230 Ala Ala Ala Ala Lys Ala Thr Gln Leu Ala Leu Lys Val Ala Glu 250 Thr Ala Val Lys Thr Glu Ala Asp Ala Ala Ala Ala Val Ala Ala Ala Lys Ala Arg Ala Val Ala Asp Ala Ala Ala Ser Arg Ala Thr Ala 280 Val Asn Ala Ile Ala Glu Ala Glu Glu Arg Asp Ser Ala Gln Ala Glu 295 Asn Thr Ala Gly Val Ala Gln Ala Ala Leu Ala Ala Ala Glu Ala Gln Asp Ser Cys Ile Gly Ala Ala Ala Thr Pro Arg His Ser Ser Tyr Ala Trp Trp Lys Leu Arg Ile Thr Ser Leu Ile Val Ile Leu Ser Pro Arg Asn Arg Arg Thr <210> SEQ ID NO 30 <211> LENGTH: 422 <212> TYPE: PRT <213 > ORGANISM: Bombus terrestris <400> SEQUENCE: 30 Gly Asn Ser Glu Ser Gly Glu Asn Trp Lys Asn Gly Glu Ser Ser Glu 10 Ser Gly Lys Asn Trp Arg Asn Ser Gly Ser Ser Glu Ser Gly Lys Asn Trp Lys Asn Gly Gly Ser Ser Glu Ser Asn Lys His Trp Lys Asn Gly Gly Ser Ser Glu Ser Gly Glu Lys Trp Lys Asn Ser Glu Ser Ser Glu

Ala Leu Ala Ser Lys Ser Glu Ala Leu Thr Ser Glu Ala Glu Ile Ala

	50					55					60				
Ser 65	Gly	Lys	Asn	Trp	Lys 70	Asn	Ser	Gly	Ser	Ser 75	Glu	Ser	Gly	ГÀз	Asn 80
Trp	Lys	Asn	Gly	Gly 85	Ser	Ser	Glu	Ser	Asn 90	Lys	His	Trp	ГÀз	Ser 95	Gly
Gly	Ser	Ser	Glu 100	Ser	Gly	Glu	Lys	Trp 105	Lys	Asn	Ser	Glu	Ser 110	Gly	Asn
Lys	Gly	Lys 115	Ser	Ser	Lys	Ser	Ser 120	Glu	Ser	Trp	Lys	Ser 125	Asn	Glu	Asn
Ser	Lys 130	Asn	Asp	Gly	Ser	Trp 135	Lys	Ser	Ser	Glu	Glu 140	Ser	Glu	Lys	Trp
Lys 145	Asp	Gly	Lys	Ala	Val 150	Ala	Glu	Asp	Ser	Val 155	Ser	Ile	Asn	Trp	Ala 160
Asp	Val	Lys	Glu	Gln 165	Ile	Ser	Asn	Ile	Ala 170	Thr	Ser	Leu	Glu	Lys 175	Gly
Gly	Asn	Leu	Glu 180	Ala	Val	Leu	Lys	Ile 185	Lys	Lys	Gly	Glu	Lys 190	Lys	Ile
Ser	Ser	Leu 195	Glu	Glu	Ile	ГЛа	Glu 200	ГÀв	Ile	Ser	Val	Leu 205	Leu	Lys	Trp
Ile	Gln 210	Glu	Gly	ГÀа	Asp	Thr 215	Ser	Ser	Leu	Leu	Asp 220	Leu	Lys	Glu	Gly
Ser 225	Lys	Asp	Ile	Ala	Ser 230	Leu	Lys	Glu	Ile	Lys 235	Gly	ГÀв	Ile	Leu	Leu 240
Ile	Val	Lys	Leu	Val 245	Asn	Glu	Gly	ГÀв	Asp 250	Thr	Ser	Gly	Leu	Leu 255	Asp
Leu	Glu	Ala	Ser 260	Gly	ràs	Val	Ile	Leu 265	Glu	Leu	Gln	Ser	Ala 270	Ile	Glu
ГÀз	Val	Leu 275	Val	ràa	Ser	Glu	Lys 280	Val	Thr	Lys	Val	Ser 285	Glu	Val	Ser
Gly	Leu 290	Val	Lys	Ser	ràs	Thr 295	Val	Ser	Asp	Ile	300 TÀS	Pro	Leu	Gln	Ala
Val 305	Ile	Pro	Leu	Ile	Leu 310	Glu	Leu	Gln	ГÀа	Thr 315	Asp	Ile	Asn	Leu	Ser 320
Thr	Leu	Asn	Lys	Trp 325	Ser	Thr	Val	Asn	Val 330	Asn	Ser	Ile	Asp	Lys 335	Glu
Arg	Val	Thr	Lys 340	Thr	Val	Pro	Val	Leu 345	Leu	Gln	Ser	Met	Lys 350	Gly	Gly
Glu	Asp	Ile 355	Gln	Asn	Leu	Leu	Ser 360	Ala	Lys	Gly	Ala	Lув 365	Lys	Leu	Gly
Ile	Ser 370	Ala	Leu	Asp	Leu	Gln 375	Ala	Val	Gln	Gly	Ala 380	Leu	Gly	Val	Val
Gly 385	Lys	Leu	Ser	Ser	Gly 390	Gly	Ala	Leu	Asn	Ser 395	Lys	Gly	Leu	Leu	Asn 400
Leu	Lys	Asp	Gly	Ala 405	Ser	Val	Leu	Gly	Ala 410	Gly	Lys	Ile	Gly	Gly 415	Leu
Ile	Pro	Leu	Pro 420	Lys	Leu										
<210	)> SI	EQ II	ои с	31											

<sup>&</sup>lt;210> SEQ ID NO 31 <211> LENGTH: 927 <212> TYPE: DNA <213> ORGANISM: Bombus terrestris

agcagcgaag catggtcaat ttaa

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gctgtgaccg	ctagatccgg	acttcgtgcc	ggtcaggtag	cegtggeete	gcagaaggat	120
gccacacttc	aggcagatgc	ctcagcggcc	gccgcggccg	ctgcacgcgc	ttccgccgac	180
cagtcggcca	gtctagccca	acagtcggcg	tctttgcagt	ccaaagctgc	cgccagagca	240
aaatcagccg	aggagtcagc	ggcagctacg	gccaaagccg	agttgcaggc	agaatccatt	300
gctgcatctg	ccagttccaa	tgccagagag	gctgcagcgt	ccgcaaaagc	ctccgcatcc	360
gcgatgtcat	cggctgccgt	gcaggcgaaa	ctcgctgaaa	agacggccaa	gaatcaagct	420
ctggcttccg	aagaagccaa	actcaaggct	geegeegetg	ccagcgcagc	agcagcagcc	480
agegeegeeg	ccgaggcagc	cctgaaagct	gagagaatag	cggaagaagc	catcgccaag	540
geggeegetg	ccaaagcagc	cgccagagcc	gctgcagccg	cgttaaactc	cgcgaaggaa	600
geegeeaega	gcagcgcaag	gagegeegee	gaagccgaag	ctaagagcga	agtcgctata	660
ctgatcagcg	aactcgacaa	gaagagcagg	gaagtcgccg	cttccgcgtc	cgccaaggca	720
cgcgctgctg	ctgcggctag	ctccagaaac	gcagaaacgg	ctgttatcgg	agctaacatc	780
aatgtggcca	aagaggtctt	ggcgattccc	atcgagccaa	agaaacttcc	ggagccagag	840
ctggcgttga	aagaagagaa	tgtcgcggtc	gcgagctcag	agagtgaagt	gaaggtagaa	900
acgagcagcg	aagcatggtc	aatttaa				927
<210> SEQ 1 <211> LENG <212> TYPE <213> ORGAN	TH: 984 : DNA	s terrestri:	5			
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cagageteae	ctctgctcga	gatcgtgcag	ggtagcgcgt	cggccaccgc	atccaccgct	120
gtgaccgcta	gatccggact	tegtgeeggt	caggtagccg	tggcctcgca	gaaggatgcc	180
acacttcagg	cagatgcctc	ageggeegee	geggeegetg	cacgcgcttc	cgccgaccag	240
teggeeagte	tagcccaaca	gteggegtet	ttgcagtcca	aagctgccgc	cagagcaaaa	300
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gcatctgcca	gttccaatgc	cagagaggct	gcagcgtccg	caaaagcctc	cgcatccgcg	420
atgtcatcgg	ctgccgtgca	ggcgaaactc	gctgaaaaga	cggccaagaa	tcaagctctg	480
gcttccgaag	aagccaaact	caaggctgcc	gccgctgcca	gcgcagcagc	agcagccagc	540
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gccacgagca	gcgcaaggag	cgccgccgaa	gccgaagcta	agagcgaagt	cgctatactg	720
atcagcgaac	tcgacaagaa	gagcagggaa	gtegeegett	ccgcgtccgc	caaggcacgc	780
gctgctgctg	cggctagctc	cagaaacgca	gaaacggctg	ttatcggagc	taacatcaat	840
gtggccaaag	aggtcttggc	gattcccatc	gagccaaaga	aacttccgga	gccagagctg	900
gcgttgaaag	aagagaatgt	cgcggtcgcg	agctcagaga	gtgaagtgaa	ggtagaaacg	960

984

<210> SEQ ID NO 33 <211> LENGTH: 882 <212> TYPE: DNA <213> ORGANISM: Bombus terrestris <400> SEQUENCE: 33 cacgtggtga agcgcgacaa ggagctcaag gccccggctt taccggaact actcggtgat 60 gggtctgaca cgctcggtgc ctcgatggag aacgggatca aagtcgccag agcatcgcag 120 aatgtgggtc tgagaacaga gttgaatgca gccgcgcggg ctgcagccgc tgctgcgacc aagcaggcca aagacacaga ggccgcggaa gctggagcgg ccgctgcgat tgccatcgct ategecaage gtgaagaage tateaaagea agegaattag ceageaagtt gttgaeagee 300 360 geggetgggt ccagegaage tgcegtgtca gegaeggtga gggeggegca attgaeggee gcagctagcg cagctgccaa agcttctgca tccgcctctg aggcttctgc cgaagcccag 420 480 gtgagggcca acgccgaagc aaacatcgcc aagaaagctt cggcagctga agcaaaagcc 540 gcagccqaaq cccaggttaa ggcggaactc gccaagaaag cggccqccgg tttcttagct aaggetagae tageggeeag egeegaatee gaggeeacta aactegeage egaagetgaa 600 gtagcactgg ctaaggccag agtcgccgtc gaccagtcgc agagcgcaca ggcaaccgct 660 720 accgctcaag ctgccacage cgttcagctg cagtctcaag cagctaacgc ggaagcctcc 780 gctgtagcac aggctgaaac tctgctggtc acggcggaag ccgtctctgc cgcggaagcc gaagccgcga ccaaagctac cagttggggc gaagaatgtc atcaacgaga aaaagttacg 840 tttagcgaag atcgattaaa cgagagacaa gacaattggt ag 882 <210> SEQ ID NO 34 <211> LENGTH: 942 <212> TYPE: DNA <213 > ORGANISM: Bombus terrestris <400> SEOUENCE: 34 atgaagattc cagcaatact ggttacgtct ctgctggtct ggggtggtct ggccgagggc 60 120 cacgtggtga agcgcgacaa ggagctcaag gccccggctt taccggaact actcggtgat gggtctgaca cgctcggtgc ctcgatggag aacgggatca aagtcgccag agcatcgcag 180 aatgtgggtc tgagaacaga gttgaatgca gccgcgggg ctgcagccgc tgctgcgacc 240 aagcaggcca aagacacaga ggccgcggaa gctggagcgg ccgctgcgat tgccatcgct ategecaage gtgaagaage tateaaagea agegaattag ceageaagtt gttgaeagee geggetgggt ccagegaage tgeegtgtea gegaeggtga gggeggegea attgaeggee 420 480 gcagetageg cagetgecaa agettetgea teegeetetg aggettetge egaageecag gtgagggcca acgccgaagc aaacatcgcc aagaaagctt cggcagctga agcaaaagcc 540 gcagccgaag cccaggttaa ggcggaactc gccaagaaag cggccgccgg tttcttagct aaggctagac tagcggccag cgccgaatcc gaggccacta aactcgcagc cgaagctgaa 660 gtagcactgg ctaaggccag agtcgccgtc gaccagtcgc agagcgcaca ggcaaccgct 720 780 accqctcaaq ctqccacaqc cqttcaqctq caqtctcaaq caqctaacqc qqaaqcctcc getgtageae aggetgaaae tetgetggte aeggeggaag eegtetetge egeggaagee 840 gaagccgcga ccaaagctac cagttggggc gaagaatgtc atcaacgaga aaaagttacg 900

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acagetgegg etetggetag taccaaggea actgeageeg cagaggetaa ggeateegee	180
aaagtgaaag cttctgcctt ggccctcgct gaggctttct tgcgtgcgtc ggcagcgttt	240
gctgctgctt cagccaaagc tgctgccgct gtaaaggaag caacgcaggc acagttgctg	300
gcacaggaga aggetttgat agegttgaaa acteaatetg ageaacaage tgeetetget	360
egegeggaeg eegeggetge egeageegta teegegetag aaegegeeea ggeeteetee	420
agagcagcca cgaccgccca agacatetee agegatetgg agaaacgtgt cgccacetea	480
geogetgetg aageaggtge cacceteaga geggaacaat eegeegegea ategaaatgg	540
teegeegeac tggeegeeca aacegeeget getgeageeg etatagaage aaaggeeace	600
getteeteag aaageacege tgeegetaet agtaaggeeg eegtgttgae egetgaeaet	660
agcagegeag aagetgeege tgeageggag geacaateeg ettegeggat egeaggtaca	720
gcagccaccg agggatccgc caactgggct agcgagaact cgcgtaccgc acaactggaa	780
gcttccgcct cagcgaaggc caccgcagcc gcagctgtcg gagatggagc tattatagga	840
cttgcacggg acgctagtgc cgcagctcag gcagccgcag aagttaaagc cttagctgaa	900
gctagtgcca gcttaggtgc ttcagaaaag gacaagaaat ga	942
<210> SEQ ID NO 36 <211> LENGTH: 999 <212> TYPE: DNA <213> ORGANISM: Bombus terrestris	
<400> SEQUENCE: 36	
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aacgtggaga ctagtgcgaa gcgaaaggag aacggcgcac cgaaactcgg cgagagcaca	180
gctgcggctc tggctagtac caaggcaact gcagccgcag aggctaaggc atccgccaaa	240
gtgaaagett etgeettgge eetegetgag getttettge gtgegtegge agegtttget	300
gctgcttcag ccaaagctgc tgccgctgta aaggaagcaa cgcaggcaca gttgctggca	360
caggagaagg ctttgatagc gttgaaaact caatctgagc aacaagctgc ctctgctcgc	420
geggaegeeg eggetgeege ageegtatee gegetagaae gegeeeagge eteeteeaga	480
gcagccacga ccgcccaaga catctccagc gatctggaga aacgtgtcgc cacctcagcc	540
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gccaccgagg gatccgccaa ctgggctagc gagaactcgc gtaccgcaca actggaagct	840
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geggaaaaat egaacgaget ggegeaaget gaggetgeag eegeegeega ageeeagget	660
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caagacteet geateggege tgeegegact eetaggeatt egtegageta tgeatggtgg	960
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	ctc ggaaagcaac aaacattgga		300	
	aaa cagtgaaagc ggaaataaag cga aaactcgaag aacgacggca		420	
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	cga agggaaagac actagtggtc		780	
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Ser	Ala	Ser 35	Ala	Ser	Ala	Lys	Ala 40	Gly	Ser	Ser	Asn	Ile 45	Leu	Ser	Arg
Val	Gly 50	Ala	Ser	Arg	Ala	Ala 55	Ala	Thr	Leu	Val	Ala 60	Ser	Ala	Ala	Val
Glu 65	Ala	Lys	Ala	Gly	Leu 70	Arg	Ala	Gly	Lys	Ala 75	Thr	Ala	Glu	Glu	Gln 80
Arg	Glu	Ala	Leu	Glu 85	Met	Leu	Thr	Leu	Ser 90	Ala	Asp	ГÀв	Asn	Ala 95	Glu
Ala	Arg	Ile	Leu 100	Ala	Asp	Asp	Thr	Ala 105	Val	Leu	Val	Gln	Gly 110	Ser	Ala
Glu	Ala	Gln 115	Ser	Val	Ala	Ala	Ala 120	Lys	Thr	Val	Ala	Val 125	Glu	Glu	Glu
Ser	Ala 130	Ser	Leu	Asp	Ala	Ala 135	Ala	Val	Glu	Ala	Glu 140	Val	Ala	Ala	Ala
Thr 145	Ser	Lys	Ser	Ser	Ala 150	Gly	Gln	Ala	Leu	Gln 155	Ser	Ala	Gln	Thr	Ala 160
Ala	Ser	Ala	Leu	Arg 165	Thr	Ser	Ala	Arg	Ser 170	Ala	Leu	Thr	Ala	Leu 175	ГÀв
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Glu	Lys	Ala 195	Leu	Ala	Ala	Thr	Gln 200	Asp	Ala	Asn	Ala	Ala 205	Ala	Gln	Gln
Ala	Met 210	Ala	Ala	Glu	Ser	Ala 215	Ala	Ala	Glu	Ala	Ala 220	Ala	Ile	Ala	Ala
Ala 225	Lys	Gln	Ser	Glu	Ala 230	Arg	Asp	Ala	Gly	Ala 235	Glu	Ala	Lys	Ala	Ala 240
Met	Ala	Ala	Leu	Ile 245	Thr	Ala	Gln	Arg	Asn 250	Leu	Val	Gln	Ala	Asn 255	Ala
Arg	Ala	Glu	Met 260	Ala	Ser	Glu	Glu	Ala 265	Glu	Leu	Asp	Ser	Lys 270	Ser	Arg
Ala	Ser	Asp 275	Ala	Lys	Val	Asn	Ala 280	Val	Ala	Arg	Ala	Ala 285	Ser	Lys	Ser
Ser	Ile 290	Arg	Arg	Asp	Glu	Leu 295	Ile	Glu	Ile	Gly	Ala 300	Glu	Phe	Gly	Lys
Ala 305	Ser	Gly	Glu	Val	Ile 310	Ser	Thr	Gly	Thr	Arg 315	Ser	Asn	Gly	Gly	Gln 320
Asp	Ala	Ile	Ala	Thr 325	Ala	Glu	Ala	Ser	Ser 330	Ser	Ala	Ser	Ala	Val 335	Gly
Ile	Lys	Lys	Thr 340	Ser	Gly	His	Trp	Gly 345	Ser	Gly	Lys	Trp	Ser 350	Arg	Val
Ser	Lys	Gly 355	Lys	Gly	Trp	Ala	Ser 360	Ser	Asn	Ala	Asp	Ala 365	Asp	Ala	Ser

Ser	Ser 370	Ser	Ile	Ile	Ile	Gly 375	Gly	Leu	Lys	Arg	Gly 380	Gly	Leu	Gly	Ser
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Ser	Gly 50	Ala	Ser	Ala	Ser	Ala 55	Ser	Ala	Lys	Ala	Gly 60	Ser	Ser	Asn	Ile
Leu 65	Ser	Arg	Val	Gly	Ala 70	Ser	Arg	Ala	Ala	Ala 75	Thr	Leu	Val	Ala	Ser 80
Ala	Ala	Val	Glu	Ala 85	Lys	Ala	Gly	Leu	Arg 90	Ala	Gly	Lys	Ala	Thr 95	Ala
Glu	Glu	Gln	Arg 100	Glu	Ala	Leu	Glu	Met 105	Leu	Thr	Leu	Ser	Ala 110	Asp	Lys
Asn	Ala	Glu 115	Ala	Arg	Ile	Leu	Ala 120	Asp	Asp	Thr	Ala	Val 125	Leu	Val	Gln
Gly	Ser 130	Ala	Glu	Ala	Gln	Ser 135	Val	Ala	Ala	Ala	Lys 140	Thr	Val	Ala	Val
Glu 145	Glu	Glu	Ser	Ala	Ser 150	Leu	Asp	Ala	Ala	Ala 155	Val	Glu	Ala	Glu	Val 160
Ala	Ala	Ala	Thr	Ser 165	Lys	Ser	Ser	Ala	Gly 170	Gln	Ala	Leu	Gln	Ser 175	Ala
Gln	Thr	Ala	Ala 180	Ser	Ala	Leu	Arg	Thr 185	Ser	Ala	Arg	Ser	Ala 190	Leu	Thr
Ala	Leu	Lys 195	Leu	Ala	Arg	Leu	Gln 200	Gly	Ala	Ala	Ser	Ser 205	Asn	Ala	Ala
Arg	Met 210	Met	Glu	rys	Ala	Leu 215	Ala	Ala	Thr	Gln	220	Ala	Asn	Ala	Ala
Ala 225	Gln	Gln	Ala	Met	Ala 230	Ala	Glu	Ser	Ala	Ala 235	Ala	Glu	Ala	Ala	Ala 240
Ile	Ala	Ala	Ala	Lys 245	Gln	Ser	Glu	Ala	Arg 250	Asp	Ala	Gly	Ala	Glu 255	Ala
Lys	Ala	Ala	Met 260	Ala	Ala	Leu	Ile	Thr 265	Ala	Gln	Arg	Asn	Leu 270	Val	Gln
Ala	Asn	Ala 275	Arg	Ala	Glu	Met	Ala 280	Ser	Glu	Glu	Ala	Glu 285	Leu	Asp	Ser
Lys	Ser 290	Arg	Ala	Ser	Asp	Ala 295	Lys	Val	Asn	Ala	Val 300	Ala	Arg	Ala	Ala
Ser 305	Lys	Ser	Ser	Ile	Arg 310	Arg	Asp	Glu	Leu	Ile 315	Glu	Ile	Gly	Ala	Glu 320

Phe	Gly	Lys	Ala	Ser 325	Gly	Glu	Val	Ile	Ser 330	Thr	Gly	Thr	Arg	Ser 335	Asn
Gly	Gly	Gln	Asp 340	Ala	Ile	Ala	Thr	Ala 345	Glu	Ala	Ser	Ser	Ser 350	Ala	Ser
Ala	Val	Gly 355	Ile	Lys	Lys	Thr	Ser 360	Gly	His	Trp	Gly	Ser 365	Gly	Lys	Trp
Ser	Arg 370	Val	Ser	Lys	Gly	Lys 375	Gly	Trp	Ala	Ser	Ser 380	Asn	Ala	Asp	Ala
Asp 385	Ala	Ser	Ser	Ser	Ser 390	Ile	Ile	Ile	Gly	Gly 395	Leu	Lys	Arg	Gly	Gly 400
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Trp	Gly	Lys 35	Glu	Glu	Lys	ГЛа	Leu 40	Glu	Glu	Leu	Asp	Glu 45	Glu	Ser	Leu
Asn	Glu 50	Ala	Ala	Leu	Lys	Val 55	Gly	Ile	Lys	Asn	Gly 60	Gly	Leu	Asp	Val
Ala 65	Lys	Gly	Ala	Ala	Val 70	Leu	Glu	Ala	Ala	Met 75	Ser	Asp	Val	Ala	Thr 80
Leu	Thr	Asp	Gln	Arg 85	Ser	Leu	Val	Asp	Leu 90	Gly	Leu	Gly	Pro	Val 95	Ala
Asn	Glu	Ala	Glu 100	Ile	Leu	Ala	Glu	Ala 105	Gln	Ala	Ala	Thr	Ser 110	Ala	Gln
Ala	Gly	Ala 115	Val	Ala	Asn	Ser	Ala 120	Ala	Glu	Arg	Ala	Ile 125	Ala	Ala	Met
Glu	Met 130	Ala	Asp	Arg	Thr	Glu 135	Tyr	Ile	Ala	Ala	Leu 140	Val	Thr	Thr	Lys
Ala 145	Ala	ГÀа	Ala	Ala	Glu 150	Ala	Thr	Met	Ala	Ala 155	Thr	Ala	Arg	Ala	Thr 160
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Ala	Ala 210	Thr	Ala	Ala	Lys	Ala 215	Lys	Glu	Ser	Ala	Met 220	Lys	Ser	Leu	Ser
Ala 225	Ala	Gln	Ala	Ala	Ala 230	Lys	Ala	Gln	Ala	Arg 235	Asn	Ala	Glu	Ala	Ser 240
Ala	Glu	Ala	Gln	Ile 245	Lys	Leu	Ser	Gln	Ala 250	Arg	Ala	Ala	Val	Ala 255	Arg

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Glu	Ala	Ser	Ala 260	Glu	Ala	Gln	Ile	Lys 265	Leu	Ser	Gln	Ala	Arg 270	Ala	Ala
Val	Ala	Arg 275	Ala	Ala	Ala	Asp	Gln 280	Ala	Val	Cys	Ser	Ser 285	Gln	Ala	Gln
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Lys	Asn	Asp	Leu 340	Trp	Leu	His	Leu	Asn 345	Met	Lys	Gly	Glu	Ala 350	Lys	Ala
Glu	Gly	Glu 355	Ala	Val	Ser	Ile	Ser 360	Lys	Gly	His	Arg	Gly 365	Gly	Ile	Arg
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660 720

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Ser Val Thr Leu Ala Ala Ala Ala Glu Ala Lys Ala Ala Leu Asn 50 55 60	
Ala Gly Lys Ala Thr Val Glu Glu Gln Arg Glu Ala Leu Gln Leu Leu 65 70 75 80	
Thr Ala Ser Ala Glu Lys Asn Ala Glu Ala Arg Ser Leu Ala Asp Asp 85 90 95	
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Ala Lys Thr Val Ala Val Glu Gln Gly Ser Asn Ser Leu Asp Ala Ala 115 120 125	
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Gln Ala Leu Gln Ala Ala Gln Thr Ser Ala Ala Ala Ile Gln Thr Ala 145 150 155 160	
Ala Gly Ser Ala Leu Thr Ala Leu Lys Leu Ala Arg Lys Gln Glu Ala 165 170 175	
Glu Ser Asn Asn Ala Ala Glu Gln Ala Asn Lys Ala Leu Ala Leu Ser 180 185 190	
Arg Ala Ala Ser Ala Ala Thr Gln Arg Ala Val Ala Ala Gln Asn Ala 195 200 205	
Ala Ala Ala Ser Ala Ala Ser Ala Gly Ala Ala Gln Ala Glu Ala Arg 210 215 220	
Asn Ala Tyr Ala Lys Ala Lys Ala Ala Ile Ala Ala Leu Thr Ala Ala 225 230 235 240	

Gln Arg Asn Tyr Ala Ala Ala Lys Ala Ser Ala Ser Ala Gly Ser Val

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Val	Glu 290	Ile	Gly	Ala	Glu	Phe 295	Gly	Asn	Ala	Ser	Gly 300	Gly	Val	Ile	Ser
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Ala	Gln	Ala	Ser	Ala 325	Ser	Ala	Ser	Ala	Thr 330	Ser	Ser	Ser	Ser	Ser 335	Ser
Ser	Gly	Ile	Asn 340	Lys	Gly	His	Pro	Arg 345	Trp	Gly	His	Asn	Trp 350	Gly	Leu
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Asp 145	Ala	Ala	Ala	Ala	Glu 150	Ala	Glu	Ala	Ala	Ala 155	Ala	Ala	Ser	Arg	Val 160
Ser	Ala	Gln	Gln	Ala 165	Leu	Gln	Ala	Ala	Gln 170	Thr	Ser	Ala	Ala	Ala 175	Ile
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Gln	Glu	Ala 195	Glu	Ser	Asn	Asn	Ala 200	Ala	Glu	Gln	Ala	Asn 205	Lys	Ala	Leu
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Gly	Ser	Val 275	Val	Ala	Glu	Gln	Asp 280	Ala	Gln	Ser	Arg	Ala 285	Ala	Asp	Ala
Glu	Val 290	Asn	Ala	Val	Ala	Gln 295	Ala	Ala	Ala	Arg	Ala 300	Ser	Val	Arg	Asn
Gln 305	Glu	Ile	Val	Glu	Ile 310	Gly	Ala	Glu	Phe	Gly 315	Asn	Ala	Ser	Gly	Gly 320
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Ser 385	Ala	Ser	Ser	Tyr	Ser 390	Ser									
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Gly 1 Ala Tyr Val	Val Ser Asn Lys 50	Ile Ala Glu 35 Asn	Gly Ser 20 Leu Gly	Pro 5 Ala His	Ser Lys Val	Ala Ser Asp 55	Ser Ile 40 Val	Ala 25 Asn Ala	10 Ser Ala Lys	Ser Pro Gly	Ser Ala Ala 60	Ala Leu 45	Ser 30 Ala Val	15 Ile Val Val	Gly Gly Glu
Gly 1 Ala Tyr Val Ser 65	Val Ser Asn Lys 50	Ile Ala Glu 35 Asn	Ser 20 Leu Gly Ser	Pro 5 Ala His Gly Asp	Ser Lys Val Val	Ala Ser Asp 55 Ser	Ser Ile 40 Val Thr	Ala 25 Asn Ala Leu	10 Ser Ala Lys Thr	Ser Pro Gly Asp 75	Ser Ala Ala 60 Asp	Ala Leu 45 Ala	Ser 30 Ala Val Thr	15 Ile Val Val Leu	Gly Gly Glu Asn 80
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Val	Leu 210	Ala	Glu	Ala	Ala	Thr 215	Gly	Leu	Ser	Ala	Ser 220	Ala	Gly	Lys	Ala
Gln 225	Gln	Ser	Ala	Thr	Arg 230	Ala	Leu	Gln	Ala	Ala 235	Arg	Ala	Ala	Ala	Lys 240
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Glu	Ile	Asn	Gly	Ala 85	Pro	Asn	Ile	Gly	Leu 90	Gly	Leu	Lys	Gln	Val 95	Ser
Leu	Ala	Leu	Ala 100	Lys	Ala	Gln	Ala	Ser 105	Ala	Gln	Ser	Ser	Ala 110	Glu	Ala

Leu Ala Ile Ile Lys Lys Ile Val Ala Leu Leu Ile Ser Ala Tyr Val 120 Arg Ala Ala Glu Ala Ala Ala Arg Ala Ser Ala Glu Ala Leu Ala Thr Val Arg Ala Ala Glu Gln Ala Gln Lys Ile Ala Glu Ala Lys Gly Arg Ala Ala Ala Glu Ala Leu Ser Glu Leu Val Glu Ala Ser Gln Lys Ala Asp Ala Ala Ala Ala Gly Thr Thr Asp Ala Ile Glu Arg Thr Tyr Gln Asp Ala Arg Ala Ala Thr Ser Ala Gln Thr Lys Ala Ser Gly Glu Ala Glu Asn Ala Asn Arg Asn Ala Ala Ala Thr Leu Ala Ala Val Leu Ser 215 Ile Ala Lys Ala Ala Ser Gly Gln Gly Gly Thr Arg Ala Ala Val Asp 230 235 Ala Ala Ala Ala Ala Ala Ala Ala Leu His Ala Lys Ala Asn Ala Val Ser Gln Ala Thr Ser Lys Ala Ala Ala Glu Ala Arg Val Ala 265 Ala Glu Glu Ala Ala Ser Ala Gln Ala Ser Ala Ser Ala Ser Ala Gln 280 Leu Thr Ala Gln Leu Glu Glu Lys Val Ser Ala Asp Gln Gln Ala Ala 295 Ser Ala Ser Thr Asp Thr Ser Ala Ala Ile Ala Glu Ala Glu Ala Ala 310 Ala Leu Ala Ser Thr Val Asn Ala Ile Asn Asp Gly Val Val Ile Gly 330 Leu Gly Asn Thr Ala Ser Ser Ser Ala Gln Ala Ser Ala Gln Ala Ser 345 Ala Leu Ala Arg Ala Lys Asn Ala Arg Pro Lys Ile Lys Gly Trp Tyr Lys Ile Gly Gly Ala Thr Ser Ala Ser Ala Ser Ala Ser Ala Ser Ala Ser Ala Gln Ser Ser Ser Gln Gly Leu Val Tyr <210> SEQ ID NO 62 <211> LENGTH: 424 <212> TYPE: PRT <213 > ORGANISM: Oecophylla smaragdina <400> SEQUENCE: 62 Ser Glu Leu Val Gly Ser Asp Ala Ser Ala Thr Ala Ser Ala Glu Ala Ser Ala Ser Ser Ser Ala Tyr Gly Ser Lys Tyr Gly Ile Gly Ser Gly 25 Ala Val Ser Gly Ala Ser Ser Ala Pro Ala Ile Glu Gly Val Asn Val Gly Thr Gly Val Ser Asn Thr Ala Ser Ala Ser Ala Glu Ala Leu Ser Arg Gly

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Ala Gln A	la Val 15	Ala	Leu	Val	Glu 120	Lys	Val	Ala	Arg	Ala 125	Glu	Val	Asp
Leu Ala G 130	lu Ser	Ala	Arg	Lys 135	Ala	Thr	Arg	Leu	Ser 140	Ala	Glu	Ala	Ala
Lys Ala A 145	la Ala	Glu	Val 150	Glu	ГÀа	Asp	Leu	Val 155	Gly	Leu	Arg	Gly	Ala 160
Ala Gly L	rs Leu	Asn 165	Leu	Ala	Ala	Arg	Ala 170	Gly	Ser	Lys	Ala	Gln 175	Glu
Arg Ala A	sn Glu 180	Asp	Ser	Ile	Glu	Ala 185	Asn	Glu	Leu	Ala	Gln 190	Ala	Thr
Ala Ala A 1	la Gly 95	Ala	Glu	Ala	Glu 200	Ala	Lys	Ala	Asn	Ala 205	Ala	Gln	Glu
Ala Gly A 210	la Ser	Ala	Leu	Ala 215	Ile	Ala	Gln	Ala	Ala 220	Leu	Asn	Ile	Glu
Gln Glu T 225	nr Val	Lys	Leu 230	Thr	Arg	Gln	Ala	Gln 235	Asn	Thr	Arg	Leu	Arg 240
Ser Glu A	n Ile	Leu 245	Ala	Ala	Ala	Ser	Asn 250	Ala	Arg	Ala	Ile	Ala 255	Ser
Ala Glu A	la Glu 260	Ala	Ser	Ser	Asp	Leu 265	Asn	Asn	Arg	Ala	Asn 270	Ala	Ala
Arg Ser A	en Ala 75	Arg	Ala	Ala	Ala 280	Glu	Thr	Arg	Ala	Val 285	Ala	Thr	Glu
Ala Ala S 290	er Thr	Ala	Glu	Ile 295	Ala	Ala	Tyr	Ser	Ser 300	Ser	Glu	Lys	Gly
Glu Ile T 305	nr Asn	Pro	Gly 310	Pro	Leu	Pro	Lys	Ile 315	Val	Ser	Val	Thr	Ala 320
Gly Leu T	nr Gln	Asn 325	Glu	Ile	Ala	Gly	Ser 330	Gly	Ala	Ala	Ala	Ser 335	Ala
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Gly Ala G	ly Ala 55	Gly	Ala	Ser	Ala 360	Gly	Ala	Gly	Ala	Val 365	Ala	Gly	Ala
Gly Ala G 370	ly Ala	Gly	Ala	Gly 375	Ala	Ser	Ala	Gly	Ala 380	Ser	Ala	Gly	Ala
Asn Ala G 385	ly Ala	Gly	Ala 390	Ser	Ser	Leu	Leu	Leu 395	Pro	Gln	Ser	ГÀа	Leu 400
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Ala	Glu	Ala 35	Ser	Ala	Ser	Ser	Ser 40	Ala	Tyr	Gly	Ser	Lys 45	Tyr	Gly	Ile
Gly	Ser 50	Gly	Ala	Val	Ser	Gly 55	Ala	Ser	Ala	Ser	Ala 60	Ser	Ala	Ser	Ala
Ser 65	Ala	Ser	Ala	Ser	Ala 70	Ser	Ser	Ala	Pro	Ala 75	Ile	Glu	Gly	Val	Asn 80
Val	Gly	Thr	Gly	Val 85	Ser	Asn	Thr	Ala	Ser 90	Ala	Ser	Ala	Glu	Ala 95	Leu
Ser	Arg	Gly	Leu 100	Gly	Ile	Gly	Gln	Ala 105	Ala	Ala	Glu	Ala	Gln 110	Ala	Ala
Ala	Ala	Gly 115	Gln	Ala	Ala	Ile	Ala 120	Ala	Lys	Ser	CÀa	Ala 125	Leu	Ala	Ala
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Glu 145	Val	Asp	Leu	Ala	Glu 150	Ser	Ala	Arg	Lys	Ala 155	Thr	Arg	Leu	Ser	Ala 160
Glu	Ala	Ala	Lys	Ala 165	Ala	Ala	Glu	Val	Glu 170	Lys	Asp	Leu	Val	Gly 175	Leu
Arg	Gly	Ala	Ala 180	Gly	rys	Leu	Asn	Leu 185	Ala	Ala	Arg	Ala	Gly 190	Ser	Lys
Ala	Gln	Glu 195	Arg	Ala	Asn	Glu	Asp 200	Ser	Ile	Glu	Ala	Asn 205	Glu	Leu	Ala
Gln	Ala 210	Thr	Ala	Ala	Ala	Gly 215	Ala	Glu	Ala	Glu	Ala 220	Lys	Ala	Asn	Ala
Ala 225	Gln	Glu	Ala	Gly	Ala 230	Ser	Ala	Leu	Ala	Ile 235	Ala	Gln	Ala	Ala	Leu 240
Asn	Ile	Glu	Gln	Glu 245	Thr	Val	Lys	Leu	Thr 250	Arg	Gln	Ala	Gln	Asn 255	Thr
Arg	Leu	Arg	Ser 260	Glu	Asn	Ile	Leu	Ala 265	Ala	Ala	Ser	Asn	Ala 270	Arg	Ala
Ile	Ala	Ser 275	Ala	Glu	Ala	Glu	Ala 280	Ser	Ser	Asp	Leu	Asn 285	Asn	Arg	Ala
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Glu	Lys	Gly	Glu	Ile 325	Thr	Asn	Pro	Gly	Pro 330	Leu	Pro	Lys	Ile	Val 335	Ser
Val	Thr	Ala	Gly 340	Leu	Thr	Gln	Asn	Glu 345	Ile	Ala	Gly	Ser	Gly 350	Ala	Ala
Ala	Ser	Ala 355	Ser	Ala	Ser	Ala	Leu 360	Ala	Ser	Ala	Ser	Ala 365	Gly	Ala	Gly
Ala	Gly 370	Ala	Gly	Ala	Gly	Ala 375	Gly	Ala	Ser	Ala	Gly 380	Ala	Gly	Ala	Val
Ala 385	Gly	Ala	Gly	Ala	Gly 390	Ala	Gly	Ala	Gly	Ala 395	Ser	Ala	Gly	Ala	Ser 400
Ala	Gly	Ala	Asn	Ala	Gly	Ala	Gly	Ala	Ser	Ser	Leu	Leu	Leu	Pro	Gln

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1146

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780

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### 1-45. (canceled)

**46**. A silk polypeptide, wherein at least a portion of the polypeptide has a coiled coil structure, and wherein the polypeptide comprises an amino acid sequence which is at least 40% identical to any one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:56, SEQ ID NO:57; SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:62, or SEQ ID NO:63, and

wherein the silk polypeptide is fused to at least one other polypeptide; or

wherein the silk polypeptide is present in a silk fiber or copolymer and crosslinked to a surface of interest.

- 47. The silk polypeptide of claim 46, wherein
- the portion of the polypeptide that has a coiled coil structure comprises at least 10 copies of the heptad sequence abcdefg, and wherein at least 25% of the amino acids at positions a and d are alanine residues, or
- ii) the portion of the polypeptide that has a coiled coil structure comprises at least 10 copies of the heptad sequence abcdefg, and at least 25% of the amino acids at positions a, d and e are alanine residues.
- **48**. The silk polypeptide of claim **46** which is fused to at least one other polypeptide.
- **49**. The silk polypeptide of claim **46**, wherein the silk polypeptide is present in a silk fiber or copolymer and crosslinked to a surface of interest.
- ${\bf 50}.$  A product comprising at least one silk polypeptide of claim  ${\bf 46}.$
- **51**. The product of claim **50**, wherein the product is selected from the group consisting of: a personal care product, textiles, plastics, and biomedical products.

- **52**. A vector comprising: a polynucleotide which encodes a silk polypeptide, wherein at least a portion of the polypeptide has a coiled coil structure, and wherein the silk polypeptide comprises an amino acid sequence which is at least 40% identical to at least any one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:56, SEQ ID NO:57; SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:45, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:60, or SEQ ID NO:63; and
  - a heterologous promoter operably linked to the polynucleotide.
- **53.** A composition comprising the vector of claim **52**, and one or more acceptable carriers.
- **54.** A recombinant host cell comprising a polynucleotide which encodes a silk polypeptide, wherein at least a portion of the polypeptide has a coiled coil structure, and wherein the silk polypeptide comprises an amino acid sequence which is at least 40% identical to at least any one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:56, SEQ ID NO:57; SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:44, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:55, SEQ ID NO:66, SEQ ID NO:26, SEQ ID NO:66, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:62, or SEQ ID NO:63; and

wherein

- a) the polynucleotide is operably linked to a heterologous promoter, and/or
- b) the recombinant host cell is a bacterial, yeast or plant cell.
- **55**. The recombinant host cell of claim **54**, wherein the silk polypeptide comprises an amino acid sequence which is at least 50% identical to at least any one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:56, SEQ ID NO:57; SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:62, or SEQ ID NO:63.
- **56**. The recombinant host cell of claim **54**, wherein the silk polypeptide comprises an amino acid sequence which is at least 70% identical to at least any one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:56, SEQ ID NO:57; SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:62, or SEQ ID NO:63.
- 57. The recombinant host cell of claim 54, wherein the silk polypeptide comprises an amino acid sequence which is

- at least 80% identical to at least any one or more of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:56, SEQ ID NO:57; SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:62, or SEQ ID NO:63.
- **58**. The recombinant host cell of claim **54**, wherein the polynucleotide comprises a nucleic acid sequence which is at least 40% identical to any one or more of SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:70, SEQ ID NO:71, or SEQ ID NO:76.
- **59**. The recombinant host cell of claim **54**, wherein the polynucleotide comprises a nucleic acid sequence which is at least 50% identical to any one or more of SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:70, SEQ ID NO:71, or SEQ ID NO:76.
- 60. The recombinant host cell of claim 54, wherein the polynucleotide comprises a nucleic acid sequence which is at least 70% identical to any one or more of SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:70, SEQ ID NO:71, or SEQ ID NO:76.
- **61**. The recombinant host cell of claim **54**, wherein the polynucleotide comprises a nucleic acid sequence which is at least 80% identical to any one or more of SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:70, SEQ ID NO:71, or SEQ ID NO:76.
- **62**. The recombinant host cell of claim **54**, wherein the portion of the silk polypeptide that has a coiled coil structure

comprises at least 10 copies of the heptad sequence abcdefg, and wherein at least 25% of the amino acids at positions a and d are alanine residues.

- **63**. The recombinant host cell of claim **54**, wherein the portion of the silk polypeptide that has a coiled coil structure comprises at least 18 copies of the heptad sequence abcdefg, and wherein at least 25% of the amino acids at positions a and d are alanine residues.
- **64**. The recombinant host cell of claim **54** which is a bacterial cell.
- **65**. A process for preparing a silk polypeptide comprising cultivating the recombinant host cell of claim **54**, under conditions which allow expression of the polynucleotide encoding the polypeptide, and recovering the expressed polypeptide.

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