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9 October 2008

(54) **Title:** SYNTHETIC GENOMES

(57) **Abstract:** Methods are provided for constructing a synthetic genome, comprising generating and assembling nucleic acid cassettes comprising portions of the genome, wherein at least one of the nucleic acid cassettes is constructed from nucleic acid components that have been chemically synthesized, or from copies of the chemically synthesized nucleic acid components. In one embodiment, the entire synthetic genome is constructed from nucleic acid components that have been chemically synthesized, or from copies of the chemically synthesized nucleic acid components. Rational methods may be used to design the synthetic genome (e.g., to establish a minimal genome and/or to optimize the function of genes within a genome, such as by mutating or rearranging the order of the genes). Synthetic genomes of the invention may be introduced into vesicles (e.g., bacterial cells from which part or all of the resident genome has been removed, or synthetic vesicles) to generate synthetic cells. Synthetic genomes or synthetic cells may be used for a variety of purposes, including the generation of synthetic fuels, such as hydrogen or ethanol.

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## A CLASSIFICATION OF SUBJECT MATTER

IPC C12P 19/34( 2006 01),C12N 15/64( 2006 01),5/02( 2006 01),5/04( 2006 01),I/20( 2006 01),I/00( 2006 01),C07H 21/04( 2006 01),21/00( 2006 01)

USPC 435/91 1,91 4,91 5,325,419,252 3,254 11,536/23 1,25 3

According to International Patent Classification (IPC) or to both national classification and IPC

## B FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U S 435/91 1, 91 4, 91 5, 325,419,252 3,254 11, 536/23 1,25 3

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

## C DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	US 6,521,427 B1 (EVANS) 12 February 2003 (18 02 2003), columns 3-4, 9, and 18-21	1, 7-8, 11-38
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Y		2-6, 9-10
Y	FIUTCHISON et al Global Transposon Mutagenesis and a Minimal Mycoplasma Genome Science 10 December 1999, VoI 286, pages 2165-2169, see whole document	2-6, 9-10
Y	SMITH et al Generating a synthetic genome by whole genome assembly PhiX 174 bacteriophage from synthetic oligonucleotides Proc Natl Acad Sci 23 December 2003, VoI 100, No 26, pages 15440-15445, see whole document	2-6, 9-10
Y	CHECK, E Venter aims for maximum impact with minimal genome Nature 28 November 2002, VoI 420, page 350, see whole document	2-6, 9-10



Further documents are listed in the continuation of Box C

## D

See patent family annex

* Special categories of cited documents	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

09 June 2008 (09 06 2008)

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**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons

- 1  I Claims Nos  
because they relate to subject matter not required to be searched by this Authority, namely
  
- 2  Claims Nos  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically
  
- 3  Claims Nos  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6 4(a)

**Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows  
Please See Continuation Sheet

- 1  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
- 2  As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees
- 3  I As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos
  
- 4  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims, it is covered by claims Nos

**Remark on Protest**

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee
- D The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation
- No protest accompanied the payment of additional search fees

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**BOX III OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13 1 In order for all inventions to be examined, the appropriate additional examination fees must be paid

Group I, claim(s) 1-31 and 33, drawn to the special technical feature of a method for constructing a synthetic genome, including a eukaryotic cellular organelle genome

Group II, claim(s) 35-36, drawn to the special technical feature of a method for making a synthetic cell

Group III, claim(s) 38, drawn to the special technical feature of a method

Group IV, claim(s) 32, 34, and 37, drawn to the special technical feature of a synthetic genome and a synthetic cell

This application contains claims directed to more than one species of the generic invention These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13 1

In order for more than one species to be examined, the appropriate additional examination fees must be paid The species are as follows

Species A) eukaryotic cellular organelle synthetic genome

Species B) bacterial synthetic genome

The claims are deemed to correspond to the species listed above in the following manner

Species A) recited in claim 7

Species B) recited in claim 8

The following claim(s) are generic 1

The technical feature linking groups I-IV is a synthetic genome The inventions listed as Groups 1-IV do not relate to a single general inventive concept under PCT Rule 13 1 because, under PCT Rule 13 2, they lack the same or corresponding special technical features for the following reasons

According to PCT Rule 13 2 unity of invention exists only when there is a shared same or corresponding special technical feature among the claimed inventions The methods of Groups I-III and the synthetic genome and cell of Group IV share no special feature as the synthetic genome and cell of Group IV is not required to have been produced by the method of any of Group I, II, and/or III

According to PCT Rule 13 2 unity of invention exists only when the shared same or corresponding special technical feature is a contribution over the prior art The inventions of Groups I-IV do not relate to a single general inventive concept because they lack the same or corresponding special technical feature The technical feature of Groups I-IV is a synthetic genome and cell, which is shown by Evans

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(US Patent 6,521,427) to lack novelty or inventive step because Evans teaches a synthetic genome and cell (see columns 30-32) and does not make it a contribution over the prior art

37 CFR 1475 does not provide for the inclusion of multiple methods of use within the main invention. Accordingly, the methods of Groups II and III do not have unity of invention with the synthetic genome and cell of Group IV

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons. Species A) and Species B) are shown by Evans (US Patent 6,521,427) to lack novelty or inventive step because Evans teaches a synthetic genome and cell, wherein the synthetic genome can be eukaryotic or bacterial (see, e.g., column 3, bottom) and does not make it a contribution over the prior art

Continuation of B. FIELDS SEARCHED Item 3:

MEDLINE, AGRICOLA, CAPLUS, WPIDS, EMBASE, SCISEARCH, EAST, PROQUEST

search terms (minimum OR minimal), (synthetic OR man-made OR synthesis), (genome OR chromosome OR chromosomal OR genomic)