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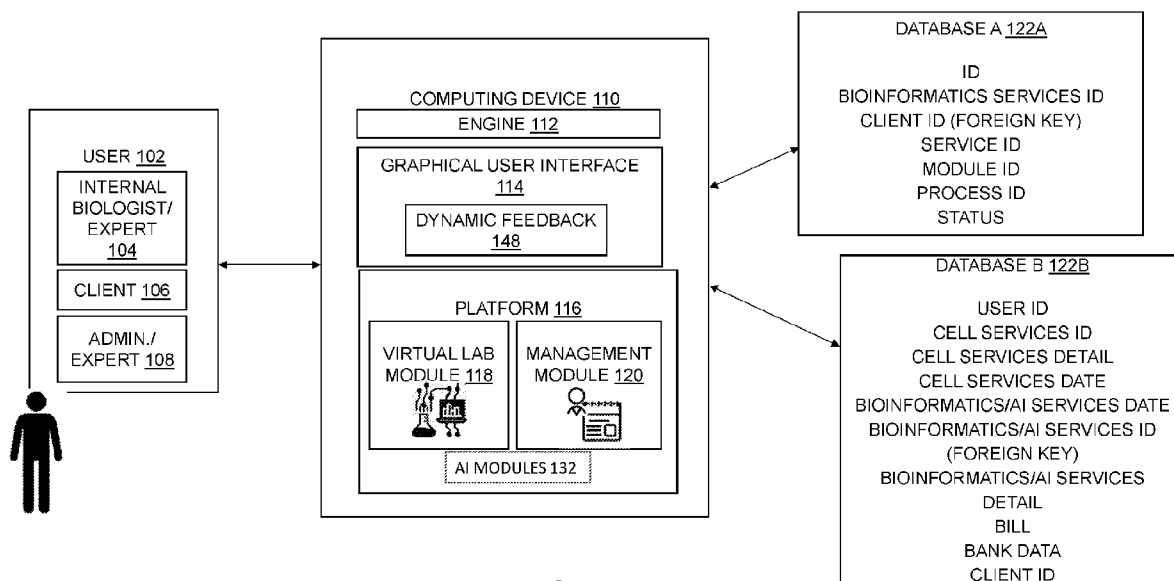


FIG. 1

(57) Abstract: The present invention provides a method to obtain unique cell lines for various applications and systems and methods for a machine learning/AI/Deep Learning software platform that supports the development and optimization of functional ingredients and solutions for the Biotech and Foodtech industries.

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**NOVEL CELL LINES AND SYSTEMS AND METHODS FOR A MACHINE LEARNING
MANUFACTURING SOFTWARE PLATFORM THAT SOURCES UNIQUE FUNCTIONAL
INGREDIENTS AND SOLUTIONS FOR THE BIOTECH AND FOODTECH INDUSTRIES**

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The present invention claims priority under 35 USC 119(e) to US Provisional Application No. 63/344,051, filed May 20, 2022, the entire contents of which is incorporated by reference in its entirety.

10 **Field of the Invention**

The field of the invention and its embodiments relate to cell lines, cell culture and systems and methods for a machine learning manufacturing software platform that optimizes cell culture, functional ingredients and solutions for the Biotech and Foodtech industries.

Background of the Invention

15 The lack of novel cell lines (defined population of cells that can proliferate multiple times *in vitro*) and the lack of affordable smart-tools (needed to fully exploit the stem cell technology) is preventing the progress and innovation of whole industries and applications. Cell lines are either used as models in the Biotech sector to test new drugs on them or as a key ingredient in the cultivated meat field (meat from animal stem cells).

20 However, most widely used cell lines were approved decades ago and are no longer fit for purpose. That is because they have one or more of the following issues:

- show batch to batch variability
- are not from relevant animal species
- do not provide the biomass in the scales that are needed nor the tissues
- 25 -have high cell culture costs associated with them
- have lack of data on their behavior at different production scales.

This results in long R&D times and costs, introducing variabilities and unexpected cell behavior. Moreover, most of these cells do not live long enough to scale up production. In addition, there is a need to reduce production costs. Scaling up production demands the use of predictive models
30 as this is a multifactor and multivariable challenge. Mid-size companies need to be able to access affordable and trustworthy AI (artificial intelligence) and this is currently lacking in the market. Hence production is centralized and costly.

In the Biotech sector, \$1.5B and an average of 12 years are spent developing new drugs (some costing the end consumer \$20k/month for a drug). The current cell lines are no longer fit for this purpose because most of them are non-relevant or they are inaccurate models for testing human diseases. Also, currently available cell lines can be an unstable and inconsistent material to work with, adding variability due to their unexpected cell behavior. This results in long R&D times and high costs (testing on non-relevant cell lines becomes more expensive and time consuming than it needs to be). Ultimately, this leads to avoidable deaths, social divide, and increases Governments' health expenditures.

In the Food sector (considered as a potential upside), the inability to scale-up cell culture in a cost-effective way is a problem as it is preventing sustainable cell-based meat products from reaching the market. Cultivated meat would reduce the increasing need for intensive animal husbandry and reduce adverse effects to the climate (animal husbandry accounts for ~14% of the GHG (greenhouse gas) emissions).

To address these problems, one solution is the development of proprietary novel cell lines and robust, affordable smart tools allowing for industrial batch to batch product consistency and faster turnaround for efficient manufacturing. These solutions also overcome difficulties associated with bringing new drugs to the market and animal husbandry issues by attaining drug cost reduction as well as providing scalability of sustainable cell-based meats, precision fermentation, and cell therapy and other applications where for example, off the shelf cell lines are particularly needed.

Depending on the application and user's need, the company develops and service off the shelf as well as customized cell lines. The AI platform and tools support the optimization of the cell lines' development, cell culture process optimization and general ingredients and solutions to scale-up production in these industries in a more efficient way.

Review of related technology:

US20220112468A1, CN114269899A, and WO2021005378A1 describe methods of reprogramming a somatic cell that includes: culturing the somatic cell in the presence of one or more Yamanaka factors and culturing the somatic cell in the absence of said one or more Yamanaka factors. These references further relate to a reprogrammed somatic cell produced according to the methods.

US20210189352A1 describes a method of preparing a population of iPS cells including (i) expressing one or more Yamanaka factors (e.g., Oct3/4, Sox2, Klf4, c-Myc, Nanog and/or Lin28) and reducing the amount and/or activity of Menin (Men1) in a population of target cells, and

(ii) optionally isolating the iPS cells from the target cell population; and a method of enhanced differentiation of a first cell into a somatic cell of a tissue of interest, including (i) treating a cell with a differentiation factor of the tissue of interest, and (ii) reducing the amount and/or activity of Menin (Men1) in a population of target cells.

5 WO2020242195A1 describes feline Wharton's jelly-derived stem cells and a preparation method therefore.

US10435711B2 describes a synthetic mRNA based reprogramming vector for the creation of human and non-human primate induced pluripotent stem cells (iPSCs) through a controlled process. Specifically, this disclosure relates to establishing combinations of reprogramming factors, including
10 fusions between conventional reprogramming factors with transactivation domains, optimized for reprogramming various types of cells. More specifically, the exemplary methods disclosed in this patent can be used for creating induced pluripotent stem cells from various mammalian cell types, including human fibroblasts. Human specific vector systems can be specifically adapted to animal cells for their successful reprogramming.

15 US9567564B2 describes human progenitor cells that are extracted from perivascular tissue of the human umbilical cord. The progenitor cell population proliferates rapidly, and harbors osteogenic progenitor cells and MHC-/- progenitor cells, and is useful to grow and repair human tissues including bone.

CN104762256A describes a method for extracting mesenchymal stem cells from umbilical
20 cord Wharton's jelly. The method comprises numerous steps, such as: separating the Wharton's jelly, digesting the Wharton's jelly, centrifugally separating the liquid after being digested, processing the separated liquid at low temperature, centrifugally separating the liquid after being processed at low temperature, culturing and the like.

WO2010013359A1 describes a method of producing iPS (induced pluripotent stem) cells,
25 comprising bringing a nuclear reprogramming substance into contact with dental pulp stem cells.

WO2009144008A1 describes a method for generating an iPS cell comprising:
introducing into a target cell one or two coding sequences each giving rise upon transcription to a factor that contributes to the reprogramming of the target cell into an induced pluripotent stem cell and selected from Oct3/4 or a factor belonging to the c-Myc, Klf4 and Sox families of factors.

30 The target cell endogenously expresses at least the factors that are not encoded by the coding sequences to be introduced and selected from Oct3/4 or factors belonging to the c-Myc, Klf4 and Sox families of factors. The cell resulting from the introduction of the one or two coding sequences

expresses the combination of factor Oct3/4 and at least one factor of each family of factors is c-Myc, Klf4 or Sox.

US20090227032A1 describes a nuclear reprogramming factor having an action of reprogramming a differentiated somatic cell to derive an iPS cell. The reference also describes the
5 aforementioned iPS cells, methods of generating and maintaining the iPS cells, and methods of using the iPS cells.

Various similar systems and methods exist in the art. However, their means of operation are substantially different from the present disclosure, as the other inventions fail to solve most of the problems enumerated by the present disclosure.

10 Summary of the Invention

The present invention and its embodiments relate to novel cell lines (with a unique reprogramming strategy) and systems and methods for a machine Learning and/or AI digital manufacturing software platform that optimizes cell lines, cell culture and functional ingredients and solutions for the Biotech and Foodtech industries.

15 An example embodiment of the present invention describes novel cell lines and a system. The system includes a platform, at least one database, and a computing engine or device and/or at least one AI/ML module. The platform includes one or more modules and one or more services. The computing device includes, at least, an engine comprising at least one artificial intelligence (AI) algorithm, machine learning or bioinformatic algorithm and a graphical user interface (GUI). The
20 GUI is configured to receive login credentials from a user (e.g., an internal biologist/expert, a client, and/or an administrator/expert) to access the platform.

In an embodiment, the platform is integrated with a Software Architecture AI stand alone program and/or for Human-AI Teaming in Smart Manufacturing including, but not limited to: ML engines, ML experimentation, IoT production line systems, and any of a plurality of other systems.

25 Then, the engine is configured to compare the login credentials to information stored in the at least one database, identify an access level to the platform associated with the user (e.g., an unrestricted access level or a restricted access level), and allow the user to interact with the platform based on the identified access level. The engine is also further configured to provide, via the GUI, dynamic and/or real-time feedback to the user (depending on the tool).

30 Moreover, the at least one database is configured to store identification information, bioinformatics service identification information, client identification information, service identification information, module identification information, process identification information,

status identification information, user identification information, cell services identification information, cell service detail information, cell service date information, bioinformatics service date information, bioinformatics/AI services detail information, bill information, and/or bank data.

The modules include a virtual lab module, a management module, a Research and Development module, Fitting monitoring & QA/QC module, a Tools module, and a Product Design module. The virtual lab module allows the user to run bioinformatics/AI processes. It should be understood that when bioinformatics is referenced herein, AI processes are also contemplated, and vice versa because one aspect of the present invention is a machine learning platform. The management module allows for the management of billings, services, experiments, and customers. In an example where the user is a biologist, the Research and Development module allows the user to upload information about experiments he/she would like to run and retrieve best protocols for the experiments. Further, in the scenario where the user is the biologist, the Fitting monitoring & QA/QC module allows the user to upload information about conditions of his/her current experiments and receive feedback for optimal parameters to be adjusted and how far from ideal they are. Moreover, the Tools module includes multiple useful tools for data analysis and visualization, including packages for analyzing images, evolutionary analysis, cell characterization, etc.

Further, in examples, each module of the one or more modules feeds AI models to provide the user with personalized answers to their questions and designs. Features or data persisted via the modules include cell growing conditions, target genes, omics, multiomics, cell typing, image processing, imaging/cell health, culture analysis, gene expression, plant properties, plant flavors, plant composition, cell biomass as an additive, and/or mixtures properties and composition calculation(s).

Additionally, the services described herein include a Molecular Farming/Plant Breeding service, a Stem Cell service, and a Food Design service. The Molecular Farming/Plant Breeding service allows the user to retrieve efficient protocols for transfecting plant cells, creating initial plants/explants, monitoring growth of the plants/explants, engineering and optimizing the expression of relevant components (e.g., animal/human proteins) in those plants/explants and predicting the best conditions for growth and replication of the plants/explants. The Stem Cell service allows the user to design protocols to reprogram, grow, engineer and/or differentiate stem cells, adjust environmental parameters, and allows the user to predict stem cell behavior *in vitro* to perform any of a plurality of purposes, for example, to scale up production. Both the Molecular Farming/Plant Breeding and Stem cell services can support reducing cell culture media costs by utilizing the proprietary “Omics

module” (adding/replacing raw ingredients based mainly on NGS (next generation sequencing), target discovery, detecting relevant metabolic pathways and by activating/deactivating those using miRNAs (micro RNAs), proteins and relevant modulators or ligands). In addition, the Omics module is linked to the proprietary “Image module” automatically connecting the cell physiology and morphology, their transformation at various stages, production scales and culture conditions to Omics and/or multiomics, which is a novel approach. The Image module allows retrieval of several cell/colony health features (when cell(s) is mentioned colony(ies) are contemplated and *vice versa*) from images and powered by AI models. In an embodiment, a Synthetic Data Production module is able to overcome the lack of publicly available stem cell data and generate data by using a bioinformatic perspective and AI. This Synthetic Data Production module (a GAN based model that is commonly applied to images and in this case has been translated to Omics related data) to date has proven to produce superior results relative to methods known in the art, such as “SMOTE” and “RO” by providing affordable services in a business model that focuses on affordability, scalability, decentralization, and accuracy.

The Food Design service calculates the mix of plant components (focusing on native plant species of various regions) with and without cell biomass and returns a final mixture's nutritional value, repercussions on human and animal gut health, organoleptic properties, and/or sustainability/sourcing/supply chain and costs.

In some examples, the engine is further configured to provide, via the GUI, an output to the user. Moreover, in some examples, the output comprises at least one of a standardized protocol and a report customized to the users' bioprocess.

Brief Description of the Several Views of the Drawings

FIG. 1 depicts a block diagram of a general platform schema, in accordance with embodiments of the present invention.

FIG. 2 depicts a block diagram of a general bioinformatics platform schema, in accordance with embodiments of the present invention.

FIG. 3 depicts a block diagram of a general stem cell platform schema, in accordance with embodiments of the present invention.

FIG. 4 depicts a block diagram of a stem cell platform workflow, in accordance with embodiments of the present invention.

FIG. 5A and FIG. 5B depict block diagrams of a web API (application programming interface) for a stem cell screen, in accordance with embodiments of the present invention. FIG. 5B is a continuation of FIG. 5A.

FIG. 6 - FIG. 10 depict block diagrams of a web API for a stem cell screen, in accordance with embodiments of the present invention.

FIG. 11 is a block diagram of a computing device included within the AI platform general schema of FIG. 1, in accordance with embodiments of the present invention.

FIG. 12 - FIG. 15 depict schematic diagrams of a vector design, in accordance with embodiments of the present invention related to the cell lines.

Detailed Description of the Invention

The embodiments of the present invention will now be described with reference to the drawings. Identical elements in the various figures are identified with the same reference numerals.

Reference will now be made in detail to each embodiment of the present invention. Such embodiments are provided by way of explanation of the present invention, which is not intended to be limited thereto. In fact, those of ordinary skill in the art will appreciate upon reading the present specification and viewing the present drawings that various modifications and variations can be made thereto.

General System/Method

In general, the present invention provides unique cell lines and systems and methods for a machine learning software manufacturing platform that optimizes functional ingredients and solutions for the Biotech and Foodtech industries. Specifically, the present invention provides unique, non-GMO stem cell lines (not limited to a certain species and not limited to non-GMO) and customized, affordable AI-based services to scale-up and control cell culture production, among other applications. The *in silico* and *in vitro* blend combined with a unique community iteration approach (B2B and B2C users from the biotech and Foodtech sectors) allows the company to provide solutions to unlock the potential of cell cultivation at any scale, including at a micro scale, a small scale, a medium or pilot scale, a large scale and on an industrial level large scale. For example, the present invention contemplates shipping cell lines and protocol/know-how to users to grow/proliferate and differentiate cells from the inventors' cell lines or from others' cell lines, at any scale and/or state, for example, at an early growth state and/or for a large scale to obtain biomass and/or different types of tissues *in vitro* and/or to express relevant components using the cell lines.

The novelty of the method described herein can be seen in at least the following key areas (jointly or separated): (1) the primary cells selected, (2) the reprogramming methods and protocols,

(3) the low immunogenic vector design for transfection, (4) the non-controversial reprogramming capability of Wharton's jelly cells that endogenously express certain pluripotent transcription factors into a "pluripotent state" using mRNA technology or other technologies, (5) the signaling pathways, (6) the special media formulation to feed the cells and (7) the AI digital manufacturing platform to provide combined services like no other in the market. The present invention also relates to business methods and computer systems to accomplish tasks related to each of the above areas (including reducing costs and other beneficial effects as disclosed herein). Each of these areas will be discussed in turn herein.

Wharton's Jelly Mesenchymal Stem Cells (WJ-MSCs)

The present invention contemplates a novel method that includes reprogramming cells to create induced pluripotent stem cells or iPSCs. In an embodiment, the present invention is able to reduce costs of pluripotent stem cell line production by a careful selection of the primary cells that are used. In an embodiment, the present invention uses a platform technology that allows the establishment of WJ-MSC based cell lines (iPSCs) as a highly proliferative cell line, with desired quality attributes among them, to endogenously express some pluripotent factor/s over certain time. . One advantage of this methodology is that it allows for a shorter reprogramming procedure duration, which leads to significant time and cost savings. In an embodiment, the iPSCs are widely used in therapeutics for disease modeling, regenerative medicine, and drug discovery. According to the methods described herein, primary cells (e.g., Wharton's jelly primary cells) are taken from umbilical cords Wharton's jelly tissue of an animal (for example, from the bovine species or other species, such as human's). This process may include mechanically isolating these cells from Wharton's jelly tissue. Mechanical isolation of mesenchymal stem cells from the Wharton's jelly part of the umbilical cord is a general method to preserve mesenchymal stem cell viability.

WJ-MSCs are a class of stem cells with high differentiative potential, an immuno- privileged status and easy access for collection, and these cells raise no legal or ethical issues. Moreover, WJ-MSCs are immunomodulators, conferring an advantage in the reprogramming phase described herein. They will not "attack or destroy" the mRNA so reprogramming can be done in a more efficient and robust way. Although these cells are mesenchymal stem cells, pluripotent genes like OCT3/4, SOX2, NANOG are expressive. Wharton's jelly primary cells are immunoprivileged cells, so this makes them suitable for gene cell therapy.

Today, most new developments are performed with human cells from other sources and cell types (fibroblasts, foreskin). To provide an innovation, the present invention utilizes these cells (WJ)

for RNA-based cell reprogramming. The cells will be expanded and the reprogramming process may occur for about 15 days until the cells show pluripotent capacity. The instant invention contemplates manipulating these cells so that they show similar characteristics to embryonic stem cells.

Reprogramming Method

5 In principle, mRNA technology is a non-integrative method (meaning that the cell lines obtained are non-GMO since the mRNA does not integrate into the host cell genome). There are other reprogramming methods that are integrative (e.g., lentivirus and retrovirus based) and non-integrative (Sendai virus and episomal vector based). The latter group, Sendai virus and episomal vector-based methods, are classified as non-integrative like mRNA vector systems, but they have integration risk
10 unlike mRNA technology. The reprogramming methods and protocols used herein include mRNA technology.

Specifically, mRNA can be produced in two ways: (1) *in vitro* transcription and (2) chemical synthesis. The present invention contemplates the use of *in vitro* transcription methods and uses DNA sequences of the reprogramming genes (e.g., Yamanaka factors; however, the instant
15 technology is not limited to these genes or combination of genes). Typically, the mRNA is targeted by the host cells internal immune system and destroyed. However, the use of Wharton's jelly cells is preferable, as those cells will produce minimal to no immune responses and hence the efficiency will be higher.

Further, the reprogramming method described herein may utilize the so-called Yamanaka
20 factors or reprogramming factors, such as but not limited to Oct3/4, Sox2, Klf4, and c-Myc. These represent a group of protein transcription factors that play an important role in the creation of induced pluripotent stem cells (cells that have the ability to become almost any tissue in the body), often called iPSCs. They also control how DNA is copied for translation into other proteins.

Vector Design

The invention contemplates, but is not limited to 3 reprogramming vector structures: 1) SOX2, c-MYC, KLF4 2) OCT3/4, and/or 3) NANOG and one replicase structure. The present invention also contemplates a vector design for transfection and protocols to reprogram the cells efficiently (e.g., replicase enzymes will transfect separately and control replicative mRNA health and
30 degradation). Once an *in vitro* transcription of an appropriate DNA template (DNA template for mRNA) is retrieved, the present invention contemplates adding CoTC (cotranscriptional cleavage) and MAZ4 (a pause element) specific signals. In an embodiment, these signals are added to get a

precise mammalian gene targeting vector design (but other signals not limited to mammalian gene targeting could be added). In the presence of these signals in the gene targeting DNA vector, all of the genes in the vector are transcribed correctly. This means that RNA polymerase reads most or all of the sequences with minimum error and/or without skipping any of the sequences. With the signals of CoTC and/or MAZ4, target gene expression is under dosage control. Further, the CoTC sequences may be used to stabilize protein synthesis in Wharton's Jelly Mesenchymal Stem Cells for their efficient reprogramming.

OCT3/4 (encoded by Pou5f1, also known as OCT3/4) was first identified in mice as an ESC-specific and germline-specific transcription factor. Specifically, the present invention designed its vector(s) so that most reprogramming genes (e.g., Yamanaka factors and/or other genes and/or other protein transcription factors) except OCT3/4 are in one vector system and, for example, OCT3/4 is in a separate one. Since overexpression of the c-MYC gene (in for example, bovine and human species) cell reprogramming into pluripotent stem cells (iPSC) causes trophoblast differentiation (e.g., a non-desired outcome), the present invention controls this expression with CoTC and MAZ4. Specifically, trophoblast is the first differentiated cell lineage of mammalian embryogenesis and forms the placenta, a structure unique to mammalian development.

FIG. 12 - FIG. 15 depict schematic diagrams of the vector design described herein. Specifically, as shown in FIG. 13, the OCT4 gene is constructed separately to better control gene dosage in time. Also, the NANOG gene is constructed separately to control pluripotency maintenance in intermediate reprogrammed cells. The NANOG vector (of FIG. 14) may also be used to increase pluripotent capacity of the WJ-MSCs before reprogramming. Additionally, the mRNA reprogramming vectors along with replicase enzyme vectors will be transfected into the WJ-MSCs. The replicase vector is depicted in FIG. 15. In order to make this vector functional, reprogramming vectors should be modified with recognition sites (e.g., replicase specific untranslated sequences). In an embodiment, these sequences can be supplied by a service company/provider. In an embodiment, the provider can also produce mRNA vectors through chemical-based synthesis to insert all required sequences into the mRNA reprogramming vectors. In an embodiment, the present invention contemplates the use of non-canonical, synthetic nucleotides. In a variation, synthetic nucleotide usage in RNA vector systems may provide 5X to 40X more protein production relative to wild type nucleotides. Intracellular innate immunity resides in every cell type and that decreases gene expression, hence protein production. It is triggered by the physicochemical properties of RNA itself. Accordingly, this

methodology will produce de-immunized RNA by tuning the composition of RNA and bypassing RNA degradation by the inner cell immune system, thereby making reprogramming more efficient. In an embodiment, the present invention also contemplates using canonical (wildtype) nucleotides and a mix of non-canonical and canonical ones.

5 The promoter for controlling transcription can be any promoter that is used for an RNA polymerase. Examples of RNA polymerases are the T7, T3 and SP6 RNA polymerases. In an embodiment, the *in vitro* transcription according to the invention is controlled by a T7 or SP6 promoter. It should be appreciated that "Promoter 1" and "Promoter 2" of FIG. 12 - FIG. 15 are not limited to any particular promoters. Further, the RNA vector may comprise untranslated regions,
10 such as a polyA region. As described, the vector provider can also produce the mRNA vector through chemical synthesis, meaning that use of a promoter may not be necessary.

CRE-LOX Technology

It should be appreciated that the present invention does not contemplate use of CRE-LOX technology, but rather utilizes the basis of this technology to have better control over mRNA numbers
15 in the host cells through replicase enzyme(s) and its own unique recognition sites within reprogramming mRNA vectors. In general, the CRE-LOX technology operates on the basis of genetic manipulation of the mammalian genome by inserting lox signals and utilizes CRE enzyme binding of these lox signals. Put another way, the CRE-LOX technology is a sophisticated site-specific recombinase technology that allows DNA modification to be targeted to a specific cell type or to be
20 triggered by a specific external stimulus. CRE is a 38 kDa recombinase protein from bacteriophage P1 that catalyzes recombination between LoxP sites. In this technology, the CRE plasmid can be separately inserted into mammalian cells, making genomic manipulation possible at certain times. At Time 0 the lox plasmid is transfected into the cells, resulting in no genome change. At Time 5, when the CRE plasmid is transfected into these lox transfected cells, the CRE enzyme starts to accumulate.
25 Further, at Time 5, the CRE binds to the lox sites following transfection and genetic manipulation.

Similar to the CRE-LOX technology, in one embodiment, the present invention separates the mRNA reprogramming vector sequences and mRNA reprogramming vector replicase sequences. At Time 0, the present invention can transfect the cells with, for example, Pluripotent/Yamanaka factors. In an embodiment, at Time 5, RNA replicase is transfected into
30 the Pluripotent/Yamanaka factors transfected cells. Accordingly, the present invention in an embodiment separates the mRNA replicase enzyme vector, like the CRE enzyme vector, and transfects cells at a certain time. In this embodiment, the present invention is able to control mRNA

reprogramming vector replication at desired times and hence, protect and complete reprogramming through a continuous mRNA reprogramming vector replication.

As described in this embodiment, CoTC and replicative mRNA can be used so there would be no need to transfect cells every 24/48 hours (e.g., mRNA degradation starts at 12 hours). In an embodiment, the present invention contemplates the use of WJ-MSCs which are immunomodulators and amenable for mRNA based modifications and/or a plurality of other types of cells (fibroblasts, other MSCs, blood cells, others). In an embodiment, vectors can be transfected during alternate time periods with the alternate time periods comprising reprogramming vectors during a first time period with a vector that comprises the replicase transfected during the second time period. The first time period and the second time period may be alternated. For example, in an embodiment, one process can occur as follows: At time 0, day 0, main mRNA reprogramming vector system having SOX2, KLF4 and c-MYC will be transfected into WJ-MSC cells together with OCT3/4 and NANOG. 12 hours later, at day 1 replicase vector system will be transfected. On day 2, the cells will be rested. On day 3, the main mRNA reprogramming vector system having SOX2, KLF4 and c-MYC will be transfected into WJ-MSC cells together with OCT3/4 and NANOG. On day 4, the replicase vector system will be transfected. Days 7-10, the WJ-MSCs will start to show or show the correct pluripotent stem cell morphology (reprogramming has occurred).

Additional Examples

In an embodiment, the present invention provides processes to also endogenously induce Wharton's Jelly cells to a "pluripotent state" using mRNA technology. In addition, the present invention further contemplates use of Bioinformatics/Data Science and stem cell teams (e.g., *in vitro* and *in silico* analysis) to detect signaling pathways to replace for example, currently used bFGF (basic fibroblast growth factor)), which belongs to a class of human pluripotent stem cell protection/growth factors, and LiF (leukemia inhibitory factors), which belongs to mice, with species-specific and relevant factors (e.g., bovine factors when developing bovine cell lines). Further, the present invention contemplates use of special media formulations to feed the cells both pre- and post-reprogramming. The present invention further contemplates development of and uses organic, plant-based stem cell culture media and further contemplates the use of different cell growth supportive matrix systems.

Artificial intelligence (AI)/Bioinformatic and Platform

Additionally, the present invention contemplates stem cell *in vitro* modeling supported by AI, which will be discussed in turn. Specifically, an AI digital manufacturing bio-platform or a platform

116 is described herein that, with use of an engine 112, AI models, complex bioinformatic/AI workflows predict stem cell behavior. The methodology works on any of a plurality of scales such as from laboratory scale, to pilot scale, to large industrial scale. Though some platforms provide partial solutions to the culture growing problem, no currently available platform is able to predict culture behavior from genomic data and images combined providing a plurality of advantages including among others, the advantage of reduced cell culture media costs in more efficient ways. Moreover, none of the services are integrated with novel cell lines nor do they contemplate continuous and systemic results/data from customers' unique production systems (unlike the present invention). Therefore, there are no customized affordable AI tools available for small to mid-size companies. The platform *schema* depicted in several figures herein is unique in terms of application (drug discovery, stem cell therapy, food technology), data processing, features, and integration. In general, the platform 116 provides numerous features obtained from users' data (and publicly available sources) and integrates genomics, imaging, and biochemical analysis data for system characterization, cell culture media optimization and cost reduction, cell health quality control, and process automatization. The platform 116 further provides a blend of *in vitro* and *in silico* analysis and customized scale-up.

In an embodiment, the present invention contemplates business models and systems related to the combination of unique cell lines, systemic data gathering from users, AI affordability, flexibility scalability/compatible with industrial scale production and the ease of implementing these strategies to small to medium size companies, mixing and leveraging information/data from the Foodtech and Biotech industries, to developing and creating community systems to leverage large scale/industrial scale data, making AI tools accessible through an on line platform, as well as other beneficial effects that should be apparent from the instant disclosure. In an embodiment, the present invention contemplates using a subscription model or other model known to those of ordinary skill in the art to implement these business models, and/or systems.

In general, and as shown in FIG. 2, the platform 116 has three distinctive services: a Molecular Farming/Plant Breeding service 124, a Stem Cell service 126, and a Food Design service 128. Each of the services integrates different modules, built as independent packages that can be differentially run depending on the user's 102 needs. The platform 116 allows the user 102 to design efficient protocols for reprogramming and growing stem cells and plants, getting precise information to adjust environmental parameters and scaling-up and optimizing the cell culture processes/protocols. In its service for Food Design, the platform 116 performs calculations for the

plant mixtures to return the mixture's nutritional values and organoleptic properties. The features generated in each module will feed AI models to provide users with personalized answers to their questions and designs. In an embodiment, all of the data generated and the predictions will be stored for future improvements and/or for AI usage to generate better data.

5 In an embodiment, various users can have different access depending on who they are. Internal users (that can be experts or non technical experts such as biologists or non biologists), external users (such as customers or others) and administrators (that can, for example, be internal software developers and/or non-technical in the biological scientific area but have a computer background, or alternatively and/or additionally, managers). In a variation, internal users may have
10 access to most data, most users' data, as well as historical data.

In an embodiment, external users may have different or a different level of access. In a variation, the external users may be customers and they may have access to certain data related to their own experiments and certain AI/bioinformatic tools. In an embodiment, the internal users may or alternatively, may not have access to this experimental data.

15 In an embodiment, administrators may have access to all data (or to almost all data).

Although the present invention describes embodiments as it relates to biologists it should be understood that it does not matter if they are biologists or not. The platform can still be managed no matter what background the user possesses (however, it should be understood that a biologist might have a better understanding of the data and also a better grasp of how to use certain specific tools).

20 In a variation, the present invention distinguishes access to the platform depending on whether the user is an internal or external user.

Moreover, it should be appreciated that the platform 116, in an embodiment, is built on the following plurality of levels of analysis; these include: genomics, transcriptomics, proteomics and metabolomics, in addition to image and video analysis, using AI/ML models for predictive services,
25 for example, to predict cell behavior *in vitro*. As such, in an embodiment, the platform 116 is able to model, control, and predict stem cell behavior *in vitro* at any of a plurality of scales, including but not limited to large scales. Moreover, the platform 116 is able to: identify and/or detect genes, identify and/or detect combinations of genes, and determine how they interact with each other, determine how they interact with other proteins, discover new interactions and pathways, and find homologous and
30 orthologous proteins, ligands and modulators (miRNAs) by conducting multi-species analysis. Moreover, the platform 116, in an embodiment, is able to optimize the cell culture media in a very precise way based on an in-depth understanding of cell biology at the various productions cell states.

In addition, in an embodiment, the platform 116 is able to understand the intermediate cell states (iCSs) using image and video analysis, which may prove decisive in having and/or developing a deep understanding of stem cell behavior and hence, allow for efficient control on an epigenetic and/or genetic level for samples of any scale, including small, medium, or large including large industrial scale. In a variation, the present invention is able to use a minimal number of samples and/or sample size to analyze cell health. Accordingly, in one variation, the methodology of the present invention allows for control and prediction of stem cell behavior *in vitro* for multiple productions no matter the scale and/or bioreactor capacity. Because cells behave differently as one increases or changes, for example, the bioreactor size and/or media formulation, the present invention allows and accounts for differing cell/colony metabolisms depending on the scale and growth conditions. Moreover, in an embodiment, the software described herein may be built in Python and R languages, using open source packages integrated with the applications using web technologies.

From samples coming from different sources related to reprogramming and stem cell pluripotency, in an embodiment, the present invention contemplates analyzing correlations between genes, gene set enrichment analysis, over representation analysis, and differential expression. In an embodiment, an *ad-hoc* genetic algorithm may be used to find new target genes that might prove to be key to developing and/or differentiating pluripotent stem cells. The novelty of this approach is that it considers genes that are not annotated in gene ontology's biological processes and it considers genes not present in KEGG's pathways.

Further, in an embodiment, RNA expression of potential key genes can be later used in a general model combined with other features to predict cell behavior. New target genes, relevant to for example, programming and pluripotency, can be inferred by homology from other species. Regarding the image module analysis, in an embodiment, the platform 116 is able to retrieve more than 36 cell/colony culture image health features or more per cell culture image (there are standard features as well as features that are customized to the user's needs). The Bioinformatics/AI image module was developed, among others, by a unique strategy of culturing and tracking single colonies and/or single cells and taking RNA for RNA-seq/microarrays/qrtPCR, media analytics from those cultures (or replicas) at various points in time throughout various cell/colony passages. This important strategy is taken into account when developing the platform schema, the corresponding Bioinformatic/AI workflows and models allowing one to correlate/combine Imaging to Multiomics and/or to metadata (coming from the experts' comments) in a unique way providing outcomes on precise cell/colony behavior like no other in the market. Also, the proprietary Synthetic Data module uses GAN

(generative adversarial networks) method (originally applied to images) to create synthetic images. The novelty in this module resides in the fact that the input data comprises microarrays, and/or RNA seqs. In testing to date, it has been found that the instant model currently out-performs widely used methods such as SMOTE and RO.

5 These features are then analyzed and integrated with the AI Modules and the rest of the modules to monitor cell health and predict stem cell behavior *in vitro*. The features obtained include but are not limited to: zoning, contour direction features, global transformations, geometric moments, Fourier's descriptors, distance and angles, and histogram based features. These features allow the quantification and the monitoring of: culture confluence, dead cells quantification, cell segmentation,
10 morphology, viability status, growth, and culture status.

Part of the novelty regarding the image module resides in cell quantification automation, allowing for more precise and in a variation real-time data integration with other culture features. Other novel aspects include the advantage of not necessarily using fluorescence microscopy for certain analyses and hence not affecting and/or modifying the cell culture. As described before,
15 part of the novelty resides in the platform 116 integrating multiple variable descriptors for describing cells and/or colonies, including but not limited to cell and/or colony health, cell counting, cell-cell/colony/tissue interactions and/or cell and/or colony growth. Further, the gathering of mass data feeds the platform 116, which allows for accurate prediction of results. Because data is constantly curated from: publicly available sources, users and/or customers unique
20 production systems, the inventors' internal wet laboratories and from the Synthetic Data production module (described herein) developed to overcome the lack of stem cell data in the public domain, the platform delivers constantly improving AI/ML predictive models and results. With this input data, which is integrated and used in the relevant and appropriate bioinformatic pipeline, the present invention delivers and will deliver structure and tools that possesses more
25 trustworthiness, meaning that the AI platform and the services of the present invention improves human and animal health as well as sustainability.

In an embodiment, the present invention relates to applying AI/ML models. After retrieving bioinformatic data (for example, features extracted from images or mass spectrometry, or after a gene expression analysis) various AI/Deep Learning models are employed in the
30 platforms of the present invention.

In an embodiment, the platform can be easily integrated with other external tools or embodiments that are known in the prior art. In an embodiment, the platform can also be adapted

to complement the tools described herein. In one variation, the platform and methodologies described herein allow users to organize, share, and/or store lab data. The technologies of other AI platforms can be incorporated into the present technological platform, even if they are not related to bioinformatic data.

Moreover, at a first stage, the software described herein supports and will support development and establishment of novel stem cell lines (e.g., new iPSCs, off the shelf and customized cell lines). In a second stage, the present invention contemplates combining the novel cell lines with scientific expertise and data, which will enable users to for example, scale-up their production using stem cells. In a third stage, the platform 116 should be able to provide continuous improvement service to reduce production costs. In an embodiment, the software has an application in predicting cell culture conditions and behavior and/or helping produce new stem cell lines for various applications (e.g., in-vitro toxicology, drug discovery, personalized medicine, tissue engineering, food technology: cultivated meats, precision fermentation). In an embodiment, the software of the present invention should be able to give predictive results in areas such as described above. Moreover, the reprogramming methods, unique cell lines and the software algorithms described herein may also be used to develop products for other medical/pharmaceutical applications.

In an embodiment, the platform 116 should be able to assist experts in the following: stem cell reprogramming to establish novel robust stem cell lines, media formulation for stem cell proliferation, media formulation for stem cell differentiation, customized and in-person services that could be representative of the users' facilities as they scale-up their production, customized stem cell line development, optimized media formulations for the desired species/selected animal, and continuous improvement services, mainly concerning media development to bring production and quality control services costs down.

It should be appreciated that the platform 116 is discussed and depicted in detail herein.

General Platform Schema

FIG. 1 depicts a block diagram of a platform general *schema*, in accordance with embodiments of the present invention. Specifically, the *schema* of FIG. 1 includes a computing device 110 associated with a user 102. The user 102 may be an internal biologist/expert 104, a client 106, or an administrator/internal expert 108. The computing device 110 may be a computer, a laptop computer, a smartphone, and/or a tablet, among other examples not explicitly listed herein. FIG. 1 may also include one or more databases, such as a database A 122A and a database B 122B. Though two databases are depicted, a quantity of the databases are not limited to such. The present invention

contemplates the use of one or of a plurality of databases (i.e., equal or greater than 2).

Specifically, each of the one or more databases may house information. For example, as depicted in FIG. 1, the database A 122A may house identification information, bioinformatics service identification information, client identification information (e.g., foreign key), service identification information, module identification information, process identification information, and/or status identification information. The database B 122B may house one or more of user identification information, cell services identification information, cell service detail information, cell service date information, bioinformatics service date information, bioinformatic services identification information (e.g., foreign key), bioinformatics/AI services detail information, bill information, bank data, and/or client identification information.

The computing device 110 may comprise an engine 112 that may execute one or more processes described herein and that can use AI/ML models. In other examples, the engine 112 may be an application, a software program, a service, a cloud service or a software platform configured to be executable on the computing device

110. In an embodiment, the user 102 may interact directly with the platform 116 via a graphical user interface (GUI) 114 of the computing device 110. The user 102 may interact with the platform 116 to access modules, such as a Virtual Lab module 118 or a Management Module 120. In an embodiment, the virtual Lab Module 118 of the platform 116 allows the user 102 upload information/cell culture data and/or to run bioinformatics/AI processes. The Management Module 120 of the platform 116 may allow for the management of billings, services, experiments, and/or customers. Responsive to the user's 102 actions, dynamic feedback 148 may be displayed via the GUI 114 to the user 102.

It should be appreciated that each user 102 may have different access credentials to the platform. For example, the engine 112 may receive login credentials from the user 102. The login credentials may include one or more of a username, a password, a biometric identification means (e.g., fingerprint identification, face recognition identification, palm print identification, iris recognition, retina recognition, etc.), etc. In response, the engine 112 may compare the login credentials to confirmation stored in the one or more databases to identify the user 102.

Identification of the user 102 may include information, such as: a name of the user 102, a telephone number of the user 102, an address of the user 102, a role or a birthdate of the user 102, and an access level granted to the user 102 for the platform 116.

Examples of the access level granted to the user 102 may include full and unrestricted access or a restricted access level (e.g., the user 102 may only have limited access and abilities with

respect to the modules on the platform 116). For example, if the user 102 is identified as an internal biologist/expert 104, the user 102 may have access to all modules of the platform 116 and may be granted the ability to retrieve past experimental data from multiple customers (maintaining the corresponding confidentiality accordingly), upload and use data, others. If the user 102 is identified as a client 106, the user 102 may have access only to certain modules and/or tools of the platform 116 and may be granted authorization to post and retrieve only their past experimental data. If the user 102 is identified as an administrator/expert/internal expert 108, the user 102 may have access to all of the modules of the platform 116 and may be granted authorization to retrieve, post, update, delete, use, and/or download any deliverables, past experiments, data and/or tools.

In an illustrative example, the present invention contemplates creating/optimizing cell lines and protocols and delivering the products and services to the users. The users may be configured to test the cell lines and protocols in their facilities and input the results of these tests into the platform 116. Consistent with a machine learning approach, the results allow for the continuous development of better predictions and/or solutions.

General Bioinformatics Platform Schema

FIG. 2 depicts a block diagram of a general bioinformatics/AI platform *schema*, in accordance with embodiments of the present invention. As shown in FIG. 2, the platform 116 may include services 130 and modules 132. The services 130 may include a Molecular Farming/Plant Breeding

service 124, a Stem Cell service 126, and/or a Food Design service 128, among others. The plant breeding service 124 allows the user 102 to retrieve efficient protocols for transfecting plant cells, creating initial plants/explants, monitoring growth of the plants/explants, and predicting the best conditions for growth and replication of the plants/explants and optimize the yields of for example mammalian protein production using those plants. The Stem Cell service 126 allows the user 102 to design protocols to reprogram, grow, engineer and/or differentiate stem cells.

Moreover, the cell service 126 allows the user 102 to retrieve information to adjust environmental parameters and to predict stem cell behavior *in vitro* to scale up production. One or more engines of the Food Design service 128 calculate the mixed plant components with and without cell biomass and return a final mixture's nutritional value, organoleptic properties, the effects on human and animal gut microbiome, and scores the mixtures based on supply chain, costs, and sustainability. The modules 132 may include an R&D module 134, a fitting & monitoring module 136, a tools module 138, and/or a product design module 140,

among others (including AI/ML modules accordingly integrated with the bioinformatic pipelines and workflows). Features/data persisted via the modules 132 include but is not limited to cell growing conditions (e.g., growing factors), target genes, omics (e.g., metabolomic/proteomics data), cell typing (e.g., microarray analysis, RNA sequencing, etc.), image processing (e.g., cell viability, undesired culture outcomes), imaging/cell health (e.g., cell shapes, relation nucleus/cytosol, cell confluence/connections, layers (e.g., multi- or single), cell area, Feret's diameter, cell segmentation, and oxygenation), culture analysis (e.g., excretion profiles (e.g., O₂, CO₂, and pH), growing factors, mass spectrometry results, and media analysis), gene expression (microarrays, RNA sequencing, metabolites, etc.), plant properties, plant flavors, plant composition, cell biomass as an additive, and mixtures properties and composition calculation. As defined herein, the Feret diameter or Feret's diameter is a measure of an object size along a specified direction. In general, it can be defined as the distance between the two parallel planes restricting the object perpendicular to that direction.

An output 152 from the platform 116 may include standardized protocols and reports customized to the user's 102 bioprocess. It should be appreciated that the output 152 depends on the credentials/access level associated with the user 102. FIG. 1 and FIG. 2 may also include a web API user interface.

Stem Cell Platform Schema

FIG. 3 depicts a block diagram of a stem cell AI-based platform schema, in accordance with embodiments of the present invention. As shown in FIGs. 3 and/or 4, the stem cell platform schema also includes a web API 144. Further, the engine 112 may include one or more artificial intelligence (AI) algorithms, bioinformatic algorithms and workflows 142. In some examples, the engine 112 may also include one or more of machine learning, deep learning, AI, and/or data science algorithms.

The R&D module 134 of the stem cells service 126 may allow users to upload information about experiments they would like to run and retrieve best protocols for such experiments. The fitting and monitoring module 136 of the stem cells service 126 may allow users such as biologists and/or experts to upload information about conditions of their current experiments and receive feedback for optimal parameters to be adjusted and how far from ideal they are. The tools module 138 of the stem cells service 126 includes multiple useful tools for data analysis and visualization, including packages for analyzing images, evolutionary analysis, cell characterization, etc.

If the user 102 access the R&D module 134 and/or the fitting and monitoring module 136 of the stem cells service 126, the user 102 may be able to access the following features: lab scale, scale up/down, and large scale. Through accessing these features, the user 102 may be provided the following options: reprogramming, differentiation, proliferation, ensemble, and co-culturing.

Specifically, the features generated in each of the modules 132 will feed AI models in order to provide the user 102 with personalized answers to their questions and designs. All of the data generated and the predictions may be stored in the one or more databases (e.g., the database A 122A and/or the database B 122B) for future improvements. As shown in FiG. 3, the database A 122A may house information, such as but not limited to identification information, protocol setting information, and data processing results. The database B 122B may house identification information, input data information, and job result information. The output 152 may include a standardized protocol and/or reports. In an embodiment, some results can be accessed in an automated way, whereas others may be released or accessed after others have had a chance to access them. For example, a team of biologists, bioinformaticians and data scientists may analyze the data at any time, for example, in-real time prior to others being able to access the data. In an embodiment, the current software can be integrated with hardware creating smart-plug in devices to control and predict cell behavior in bioreactors for example, integrating the AI based image software to control and predict culture health in bioreactors using or not using microfluidics to measure variables and using bioinformatics, thereby creating new variables related to culture health.

Stem Cell Platform Workflow

FiGs. 3 and 4 depicts a block diagram of a stem cell AI based platform workflow, in accordance with embodiments of the present invention. As shown in FiG. 4, the user 102 may interact with the GUI 114 to access an interactive form 146 of the platform 116. Through the interactive form 146, the user 102 may access the R&D module 134 and/or the Fitting Monitoring and QA/QC module 136 and/or the Tools module 138 (shown in Fig 3) of the stem cell service 126. If the user 102 accesses the R&D module 134 and/or the Fitting Monitoring and QA/QC 136 of the stem cells service 126, the user 102 may be able to access one or more of the following features: lab scale, scale up/down, and/or large scale. If the user 102 accesses the lab scale feature or the scale up/down feature, the user 102 may be provided with one or more of the following options: petri/well and/or T-flask (e.g., 5 - 45 mL). If the user 102 accesses the large scale feature, the user 102 may be prompted to select a bioreactor model and volume (e.g., between 0.1 - 10000 L. or more). Also, it should be noted that there are AI modules that are on the same level as the Lab Scale, the Scale Up/Down, the Large

Scale, etc., as well as AI modules 162 on the same level as Platform 116 (note that the latter is the same in FiGs. 5 and 6).

Through accessing these features, the user 102 may be provided with one or more of the following options: reprogramming, differentiation, proliferation, ensemble, and co-culturing. In an embodiment, each option enables different inputs from the user 102 and also determines the data processing pipeline before entering an AI model and storing data in the one or more databases (e.g., the database A 122A and/or the database B 122B).

In an embodiment, the stem cells workflow platform of FiG. 4 also includes a features extraction module 150 where data uploaded by the user 102 is processed using various packages. In an embodiment, the packages include one or more of biochemical analysis, imaging processing, AI predictive services/models. The biochemical analysis packages include one or more of Omics/multiomics, culture health, and profiling. In an embodiment, the Omics/multiomics package determines the pathways, interactions, and general data for genes and proteins from a given cell type. In an embodiment, the Omics/multiomics package may be able to link with other databases, may be associated with pathway enrichment, may be associated with GO terms, and may allow for homology gene searching.

In an embodiment, the culture health package analyzes the culture protocol and/or the culture composition from empirical data and returns parameters and comparisons with the ideally grown (i.e., the best) culture. In an embodiment, the profiling package analyzes gene profiles from microarray and/or RNA sequencing results among others and returns gene targets, gene correlations, metabolic pathways, miRNAs, modulators and/or ligands for the selected species. In an embodiment, the profiling package correlates genes and differential expression (e.g., $n > 2$). Moreover, the inputs for the profiling package include one or more of an expression matrix and a complete tagging of the samples (e.g., viability, cell count, and initial cell count).

In an embodiment, the image processing packages include one or more of cell/colony health, culture health, cell/colony profiling, plant health, plant cell health, histology analysis, and fluid dynamics. In an embodiment, the cell health package determines cell viability and growth (e.g., the shape, contact, brightness, etc.) from microscopy images and returns health feature parameters. In an embodiment, the culture health package analyzes culture images and returns culture features, such as culture color, turbidity, fluid analysis, and confluence culture. In an embodiment, the cell profiling package analyzes microscopy images and returns organelles localization and protein localization. In an embodiment, the plant health package analyzes plant images to return features related to whole

plants. In an embodiment, the histology analysis analyzes tissue images and returns a match with known tissue morphologies. In an embodiment, the fluid dynamics package determines cell viability and/or cell/colony health from images and/or by measuring new variables based on microfluidics.

The AI packages may include food functionality predictions. In an embodiment, the food
5 functionality prediction takes information about plant compositions and cell based-tissue compositions and returns information regarding possible human or animal health impact, as well as data/results related to gut microbiomes. In an embodiment, the food design package includes a food properties package that calculates plant and/or cell mixtures to return the mixture's nutritional value and organoleptic properties. Features of this package include but are not limited to nutrients balance,
10 digestibility, mixture of plant nutritional properties, and organoleptic properties. In an embodiment, the input for this package includes plant names (focusing on native plant species depending on the users' production system, their location, and/or any preference they may have) and the feed includes a plant characteristic and/or characterization database.

In an embodiment, the one or more databases (e.g., the database 122A is depicted for
15 illustrative purposes) houses information, such as identification information, protocol setting information, data processing result information, and image input information. In an embodiment, the output 152 for FIG. 4 may be a standardized protocol report.

Web API for Stem Cell Screen

FIG. 5A and FIG. 5B depict block diagrams of a web API for a stem cell screen, in
20 accordance with embodiments of the present invention. FIG. 5B is a continuation of FIG. 5A. FIG. 6 - FIG. 10 depict block diagrams of a web API for a stem cell screen, in accordance with embodiments of the present invention. Specifically, the web API stem cell screen of FIG. 5A, FIG. 6, FIG. 7, FIG. 8, FIG. 9, and FIG. 10 allows the user 102 to select one or more options, such as "About," "Why us?," "Cell lines," "My labs," "Platform virtual tour," or "Get started." FIG. 5A and
25 FIG. 6 also allow the user 102 to access numerous services (e.g., the molecular farming/plant breeding 124, the stem cell service 126, and the food design service 128) of the platform 116. FIG. 5B includes information regarding cell lines and the team.

FIG. 7 allows the user 102 to view and/or add information regarding experiments and/or scale-up experiments via the stem cell service 126. It should be understood that the same modules
30 that are shown in association with Stem Cells Service 126 in FIG. 3 may also be present in FIG. 7 and/or in FIG. 8 (but not shown in these figures).

As shown in FIG. 8, in an embodiment, external users can view their past experiments and

internal users can access all/most of the past experiments and reports of the stem cell service 126.

As shown in FIG. 9, an experiment code is generated automatically as a unique identifier and may include one or more of numbers, letters, and/or a combination (e.g., "AD156222DF"). In an embodiment, the user 102 may also be able to select "batch" or "petri" or "bioreactor" for a given experiment.

FIG. 10 depicts sample outputs for the given experiment ("AD156222DF"), which may include one or more of charts, graphs, flowcharts, tables, enabling one to interrelate data giving rise to new variables related to culture health, etc.

Computer System

In an embodiment, FIG. 11 shows a block diagram of a computing device included within the platform general *schema* of FIG. 1, in accordance with embodiments of the present invention. A basic configuration 232 of a computing device 222 is illustrated in FIG. 11 with those components within the inner dashed line. In the basic configuration 232 of the computing device 222, the computing device 222 includes a processor 234 and a system memory 224, and the computing device 222 is integrated to AI. In some examples, the computing device 222 may include one or more processors and the system memory 224. A memory bus 244 may be used for communicating between the one or more processors 234 and the system memory 224. In an embodiment, this is the basic computing device that is integrated to an AI Software Architecture stand alone and/or for Human-AI Teaming in Smart Manufacturing. It contains, but is not limited to: ML Engines, ML Experimentation, IoT Production Line Systems, and/or others.

Depending on the desired configuration, the processor 234 may be of any type, including, but not limited to, a microprocessor, a microcontroller, and a digital signal processor (DSP), or any combination thereof. Further, the processor 234 may include one or more levels of caching, such as a level cache memory 236, a processor core 238, and registers 240, among other examples. The processor core 238 may include an arithmetic logic unit (ALU), a floating point unit (FPU), and/or a digital signal processing core (DSP Core), or any combination thereof. A memory controller 242 may be used with the processor 234, or, in some implementations, the memory controller 242 may be an internal part of the memory controller 242.

Depending on the desired configuration, the system memory 224 may be of any type, including, but not limited to, volatile memory (such as RAM), and/or non-volatile memory (such as ROM, flash memory, etc.), or any combination thereof. In an embodiment, the system memory 224 includes an operating system 226, one or more engines, such as the engine 112, and program data 230.

The system memory 224 may also include a storage engine 228 that may store any information or data disclosed herein.

Moreover, the computing device 222 may have additional features or functionality, and additional interfaces to facilitate communications between the basic configuration 232 and any desired devices and interfaces. For example, a bus/interface controller 248 may be used to facilitate communications between the basic configuration 232 and data storage devices 246 via a storage interface bus 250. The data storage devices 246 may be one or more removable storage devices 252, one or more non-removable storage devices 254, or a combination thereof. Examples of the one or more removable storage devices 252 and/or the one or more non-removable storage devices 254 include magnetic disk devices (such as flexible disk drives and hard-disk drives (HDD)), optical disk drives (such as compact disk (CD) drives or digital versatile disk (DVD) drives), solid state drives (SSD), and tape drives, among others.

In some embodiments, an interface bus 256 facilitates communication from various interface devices (e.g., one or more output devices 280, one or more peripheral interfaces 272, and one or more communication devices 264) to the basic configuration 232 via the bus/interface controller 256. Some of the one or more output devices 280 include a graphics processing unit 278 and an audio processing unit 276, which are configured to communicate to various external devices, such as a display or speakers, via one or more A/V ports 274.

In an embodiment, the one or more peripheral interfaces 272 may include a serial interface controller 270 or a parallel interface controller 266, which are configured to communicate with external devices, such as input devices (e.g., a keyboard, a mouse, a pen, a voice input device, or a touch input device, etc.) or other peripheral devices (e.g., a printer or a scanner, etc.) via one or more i/O ports 268.

Further, the one or more communication devices 264 may include a network controller 258, which may be arranged to facilitate communication with one or more other computing devices 262 over a network communication link via one or more communication ports 260. The one or more other computing devices 262 may include servers, the database, mobile devices, and/or comparable devices.

The network communication link is an example of a communication media. The communication media are typically embodied by the computer-readable instructions, data structures, program modules, or other data in a modulated data signal, such as a carrier wave or other transport mechanism, and may include any information delivery media. A "modulated data signal" is a signal that has one or more of its characteristics set or changed in

such a manner so as to encode information in the signal. By way of example, and not limitation, the communication media may include wired media (such as a wired network or direct-wired connection) and wireless media (such as acoustic, radio frequency (RF), microwave, infrared (iR), and other wireless media). The term "computer-readable media", as used herein, includes both storage media and communication media.

It should be appreciated that the system memory 224, the one or more removable storage devices 252, and the one or more non-removable storage devices 254 are examples of the computer-readable storage media, which may be present. The computer-readable storage media is a tangible device that can retain and store instructions (e.g., program code) for use by an instruction execution device (e.g., the computing device 222). In an embodiment, the computer storage media may be part of the computing device 222.

The computer readable storage media/medium can be a tangible device that can retain and store instructions for use by an instruction execution device. The computer readable storage media/medium may be, for example, but is not limited to, an electronic storage device, a magnetic storage device, an optical storage device, an electromagnetic storage device, and/or a semiconductor storage device, and/or any suitable combination of the foregoing. A non-exhaustive list of more specific examples of the computer readable storage media/medium includes one or more of the following: a portable computer diskette, a hard disk, a random access memory (RAM), a read-only memory (ROM), an erasable programmable read-only memory (EPROM or Flash memory), a static random access memory (SRAM), a portable compact disc read-only memory (CD-ROM), a digital versatile disk (DVD), a memory stick, a floppy disk, and/or a mechanically encoded device (such as punch-cards or raised structures in a groove having instructions recorded thereon), and any suitable combination of the foregoing. A computer readable storage medium, as used herein, is not to be construed as being transitory signals per se, such as radio waves or other freely propagating electromagnetic waves, electromagnetic waves propagating through a waveguide or other transmission media (e.g., light pulses passing through a fiber-optic cable), or electrical signals transmitted through a wire. AI may be designed as a computing source and then link it with storage. These are interdependent and bidirectional: once the system gets the data, analyses are conducted and the results are stored.

Aspects of the present invention are described herein regarding illustrations and/or block diagrams of methods, computer systems, and computing devices according to embodiments of the invention. It will be understood that each block in the block diagrams, and combinations of the

blocks, can be implemented by the computer-readable instructions (e.g., the program code). Moreover, any feature that is disclosed herein can be combined with any other feature as long as those features are not incompatible with each other.

The computer-readable instructions are provided to the processor 234 of a general purpose computer, special purpose computer, or other programmable data processing apparatus (e.g., the computing device 222) to produce a machine, such that the instructions, which execute via the processor 234 of the computer or other programmable data processing apparatus, create means for implementing the functions/acts specified in the block diagram blocks. These computer-readable instructions may also be stored in a computer-readable storage medium that can direct a computer, a programmable data processing apparatus, and/or other devices to function in a particular manner, such that the computer-readable storage medium having instructions stored therein comprises an article of manufacture including instructions, which implement aspects of the functions/acts specified in the block diagram blocks.

The computer-readable instructions (e.g., the program code) are also loaded onto a computer (e.g. the computing device 222), another programmable data processing apparatus, or another device to cause a series of operational steps to be performed on the computer, the other programmable apparatus, or the other device to produce a computer implemented process, such that the instructions, which execute on the computer, the other programmable apparatus, or the other device, implement the functions/acts specified in the block diagram blocks.

Computer readable program instructions described herein can also be downloaded to respective computing/processing devices from a computer readable storage medium and/or to an external computer or external storage device via a network (e.g., the internet, a local area network, a wide area network, and/or a wireless network). The network may comprise copper transmission cables, optical transmission fibers, wireless transmission, routers, firewalls, switches, gateway computers, and/or edge servers. In an embodiment, a network adapter card or network interface in each computing/processing device may receive computer readable program instructions from the network and forward the computer readable program instructions for storage in a computer readable storage medium within the respective computing/processing device.

Computer readable program instructions for carrying out operations of the present invention may be assembler instructions, instruction-set-architecture (ISA) instructions, machine instructions, machine dependent instructions, microcode, firmware instructions, state-setting data, configuration data for integrated circuitry, or either source code or object code written in any combination of one or

more programming languages, including an object oriented programming language such as Smalltalk, C++, or the like, and procedural programming languages, such as the "C" programming language or other similar programming languages. The computer readable program instructions may execute entirely on the user's computer/computing device, partly on the user's computer/computing device, as
5 a stand-alone software package, partly on the user's computer/computing device and partly on a remote computer/computing device or entirely on the remote computer and/or server. In the latter *scenario*, the remote computer may be connected to the user's computer through any type of network, including a local area network (LAN) or a wide area network (WAN), or the connection may be made to an external computer (for example, through the internet using an internet Service Provider).
10 In some embodiments, electronic circuitry including, for example, programmable logic circuitry, field-programmable gate arrays (FPGA), or programmable logic arrays (PLA) may execute the computer readable program instructions by utilizing information of the computer readable program instructions to personalize the electronic circuitry, in order to perform aspects of the present invention.

15 Aspects of the present invention are described herein with reference to block diagrams of methods, computer systems, and computing devices according to embodiments of the invention. It will be understood that each block and combinations of blocks in the diagrams, can be implemented by the computer readable program instructions.

The block diagrams in the Figures illustrate the architecture, functionality, and operation of
20 possible implementations of computer systems, methods, and computing devices according to various embodiments of the present invention. In this regard, each block in the block diagrams may represent a module, a segment, or a portion of executable instructions for implementing the specified logical function(s). In some alternative implementations, the functions noted in the blocks may occur out of the order noted in the Figures. For example, two blocks shown in succession may, in fact, be executed
25 substantially concurrently, or the blocks may sometimes be executed in the reverse order, depending upon the functionality involved. It will also be noted that each block and combinations of blocks can be implemented by special purpose hardware-based systems that perform the specified functions or acts or carry out combinations of special purpose hardware and computer instructions.

Another embodiment of the invention provides a method that performs the process steps on a
30 subscription, advertising, and/or fee basis. That is, a service provider can offer to assist in one or more method/process steps described herein. In this case, the service provider can create, maintain, and/or support, etc. a computer infrastructure that performs the process steps for one or more

customers. In return, the service provider can receive payment from the customer(s) under a subscription and/or fee agreement, and/or the service provider can receive payment from the sale of advertising content to one or more third parties.

5 The descriptions of the various embodiments of the present invention have been presented for purposes of illustration, but are not intended to be exhaustive or limited to the embodiments disclosed. Many modifications and variations will be apparent to those of ordinary skill in the art without departing from the scope and spirit of the described embodiments. The terminology used herein was chosen to best explain the principles of the embodiments, the practical application or technical improvement over technologies found in the marketplace, or to enable others or ordinary
10 skill in the art to understand the embodiments disclosed herein.

When introducing elements of the present disclosure or the embodiments thereof, the articles "a," "an," and "the" are intended to mean that there are one or more of the elements.

Similarly, the adjective "another," when used to introduce an element, is intended to mean one or more elements. The terms "including" and "having" are intended to be inclusive such that there
15 may be additional elements other than the listed elements.

Although this invention has been described with a certain degree of particularity, it is to be understood that the present disclosure has been made only by way of illustration and that numerous changes in the details of construction and arrangement of parts may be resorted to without departing from the spirit and the scope of the invention. It should be understood that any feature
20 that is disclosed in the block diagrams in the drawings can be combined with any other feature that is disclosed therein (as long as they are not incompatible). When the language "one or more" is used, it should be understood that any number of possibilities from the group to which that language is directed are disclosed. All references disclosed and/or cited herein are incorporated by reference in their entireties for all purposes.

Claims

What is claimed is:

1. A system comprising:
 - a platform comprising one or more modules and one or more services;
 - at least one database; and
 - a computing device comprising at least:
 - an engine comprising at least one artificial intelligence (AI) algorithm, bioinformatic or machine learning algorithm; and
 - a graphical user interface (GUI) configured to receive login credentials from a user to access the platform;
 - the engine being configured to:
 - compare the login credentials to information stored in at least one database; identify an access level to the platform associated with the user; and
 - allow the user to interact with the platform based on the access level.
2. The system of claim 1, wherein the user is selected from the group consisting of: internal biologist/expert, client, administrator/internal expert.
3. The system of claim 1, wherein the at least one database is configured to store information selected from the group consisting of: identification information, bioinformatics/AI service identification information, client identification information, service identification information, module identification information, process identification information, status identification information, user identification information, cell services identification information, cell service detail information, cell service date information, bioinformatics/AI service date information, bioinformatics/AI services detail information, bill information, and bank data.
4. The system of claim 1, wherein the engine is further configured to provide, via the GUI, dynamic feedback to the user.
5. The system of claim 1, wherein the access level is selected from the group consisting of: an unrestricted access level and a restricted access level.

6. The system of claim 1, wherein each module of the one or more modules is selected from the group consisting of a virtual lab module, a management module, a research and development module, a fitting monitoring and QA/QC module, a tools module, and a product design module.

7. The system of claim 6, wherein the virtual lab module allows the user to run Bioinformatics/AI processes.

8. The system of claim 6, wherein the management module allows for management of billings, services, experiments run, and customers.

9. The system of claim 6,
wherein the user is a biologist and/or expert, and
wherein the research and development module allows the user to: upload information about experiments run; and
retrieve best protocols associated with the experiments.

10. The system of claim 6,
wherein the user is a biologist/expert, and
wherein the fitting and monitoring module allows the user to:
upload information about conditions of experiments; and
receive feedback for how far the conditions of the experiments need to be adjusted to coincide with optimal parameters.

11. The system of claim 6, wherein the tools module comprises tools for data analysis, and/or for visualization, and packages for analyzing images, for evolutionary analysis, for cell media optimization and/or for cell and/or colony characterization.

12. The system of claim 6, wherein each module of the one or more modules feeds AI models to provide the user with personalized answers to user questions and designs.

13. The system of claim 6, wherein features or data persisted via at least one module of the one or more modules include cell/colony growing conditions, target genes, gene discovery, omics, cell/colony typing, image processing, colony health, cell culture media analysis, cell media cost reduction, , gene expression, plant properties, plant flavors, plant taste, plant composition, cell biomass as an additive, mixtures properties, composition calculations, connecting omics/multiomics to imaging of single colonies and/or cells, colonies and/or cells interacting with each other in a plurality of conditions, 2D and 3D culture, scaffolds, , media analytics, media costs, cell culture scalability, cell culture optimization, and human and animal gut microbiome health.

14. The system of claim 1, wherein each service of the one or more services of the platform comprise a Molecular Farming/ Plant Breeding service, a Stem Cell service, or a Food Design service.

15. The system of claim 1, wherein the system allows the user to perform one or more of the following:

select primary cells, create and/or develop reprogramming methods and protocols, design low immunogenic vectors for transfection, develop and/or create a reprogramming capability for Wharton's jelly cells that endogenously express certain pluripotent transcription factors into a "pluripotent state" using mRNA technology, create and/or develop special media formulations to feed the primary cells, and/or create an AI digital manufacturing platform to provide combined services.

16. The system of claim 14, wherein the stem cell service allows the user to:

design protocols to reprogram, grow, engineer the cell to produce a compound of interest, and optimize a yield of the compound and differentiate stem cells;

retrieve information to adjust environmental parameters associated with the protocols;

and

predict stem cell behavior *in vitro* to allow a scale-up in production.

17. The system of claim 14, wherein the food design service is configured to: calculate and mix plant components with cell biomass;

calculate and mix plant components without the cell biomass; and

return results on a final mixture nutritional value, gut microbiome impact, organoleptic properties on final product and supply chain, sustainability implications, and costs implications.

18. The system of claim 1, wherein the engine is further configured to provide, via the GUI, an output to the user.

19. The system of claim 18, wherein the output comprises at least one of a standardized protocol and a report customized to the users' unique bioprocess/production system.

20. The system of claim 13, wherein the imaging is obtained when the colonies and/or cells are grown in suspension, grown using microcarriers or grown in scaffolds.

21. The system of claim 20, wherein the media costs are reduced by activating or deactivating relevant pathways and/or ingredients are replaced based upon sustainability.

22. A method of optimizing functional ingredients and solutions on cell health and cell growth for the biotech and/or foodtech industries, said method comprising:

procuring a platform comprising one or more modules and one or more services;
at least one database; and
a computing device comprising at least:
an engine comprising at least one artificial intelligence (AI) algorithm, bioinformatic or machine learning algorithm; and
a graphical user interface (GUI) configured to receive login credentials from a user to access the platform; wherein the user accesses the platform, which uses the AI, bioinformatic or machine learning algorithm to integrate multiple variable descriptors for describing cell and/or colony health and growth, and wherein the platform outputs on the GUI optimized functional ingredients and solutions on the cell and/or colony health and cell and/or colony growth.

23. A method of decreasing costs, increasing flexibility of scaling of cells/colonies, producing unique cell lines, and/or providing systemic data gathering from users, comprising utilizing the system of claim 1 or 14.

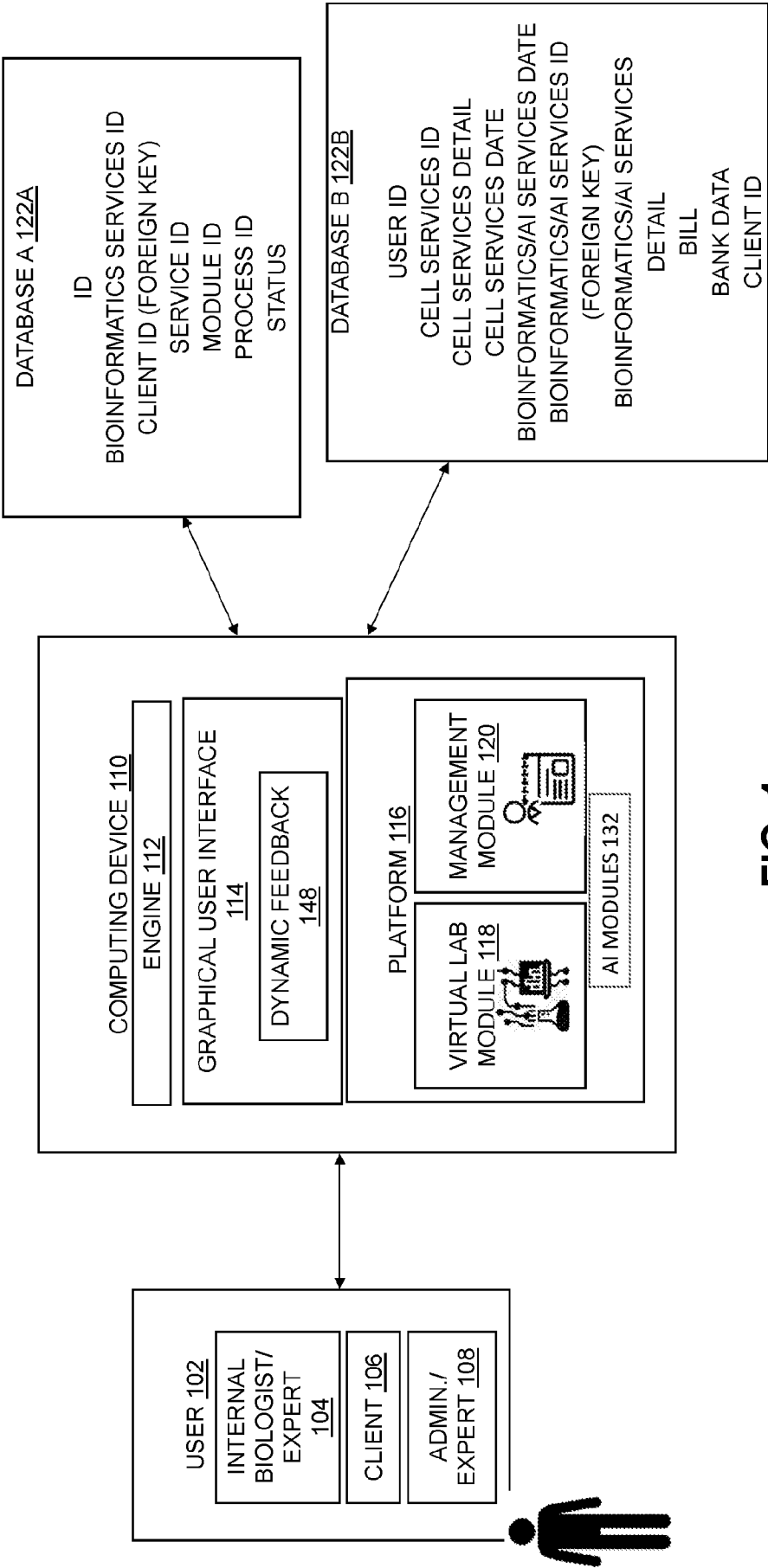


FIG. 1

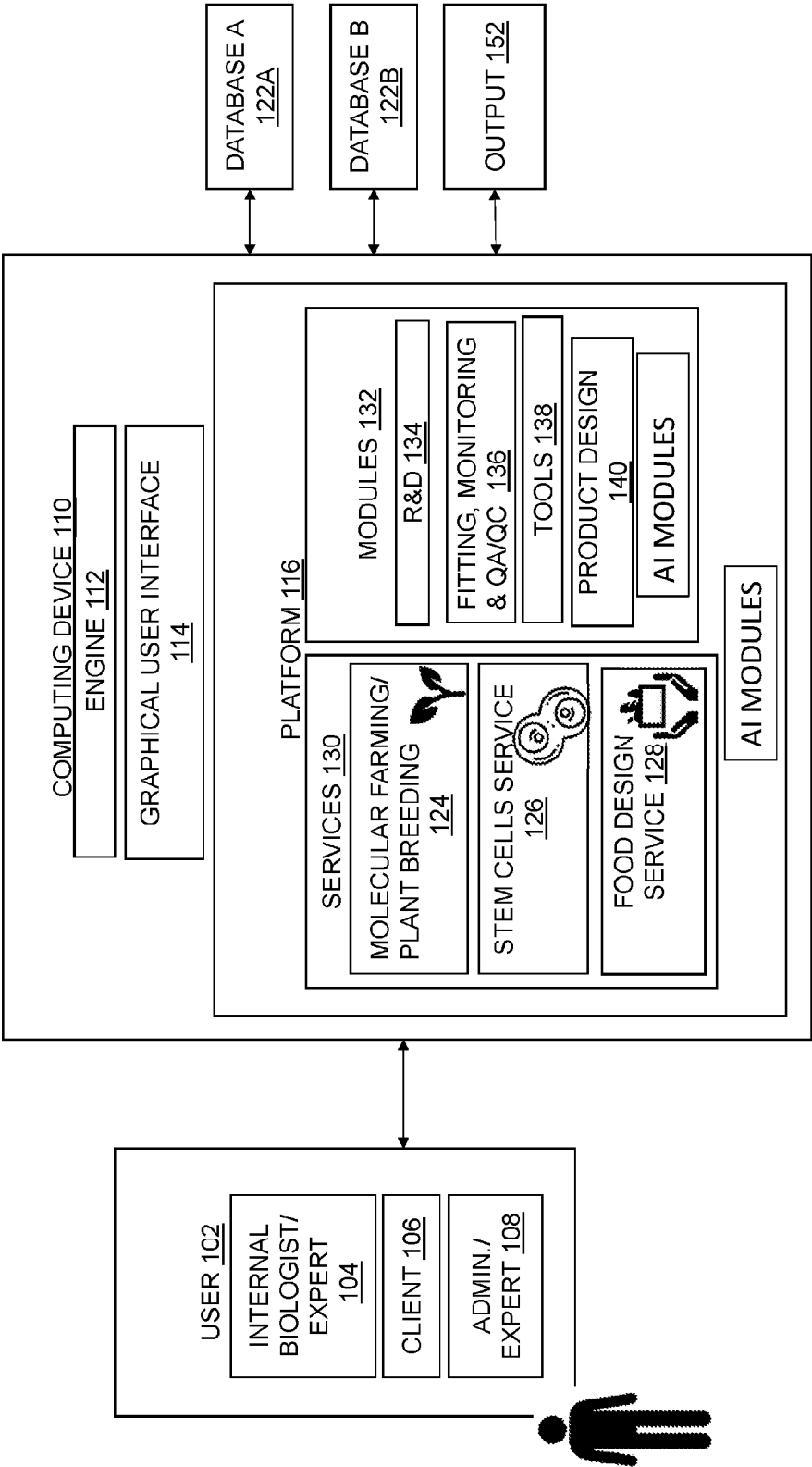


FIG. 2

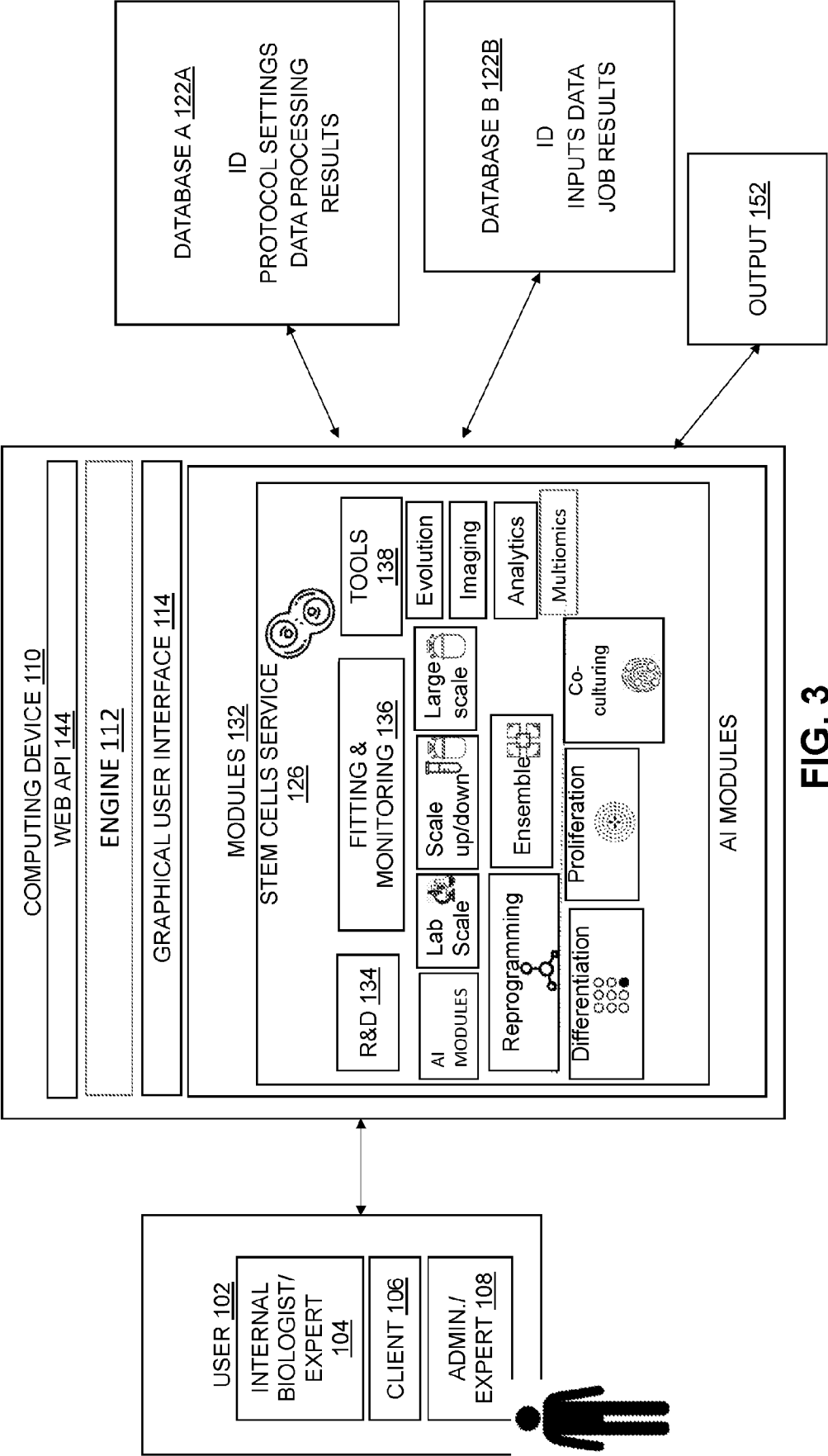


FIG. 3

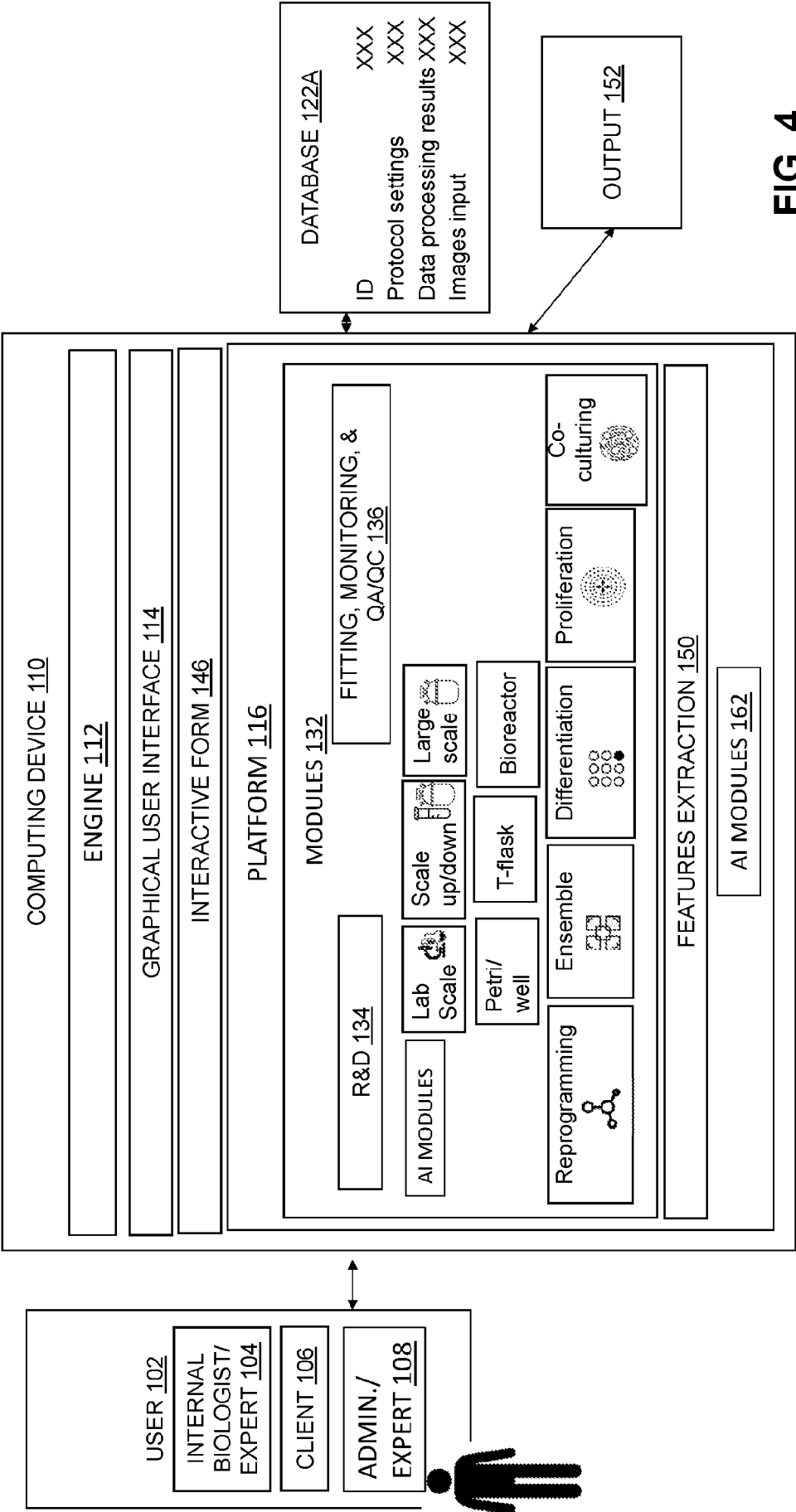


FIG. 4

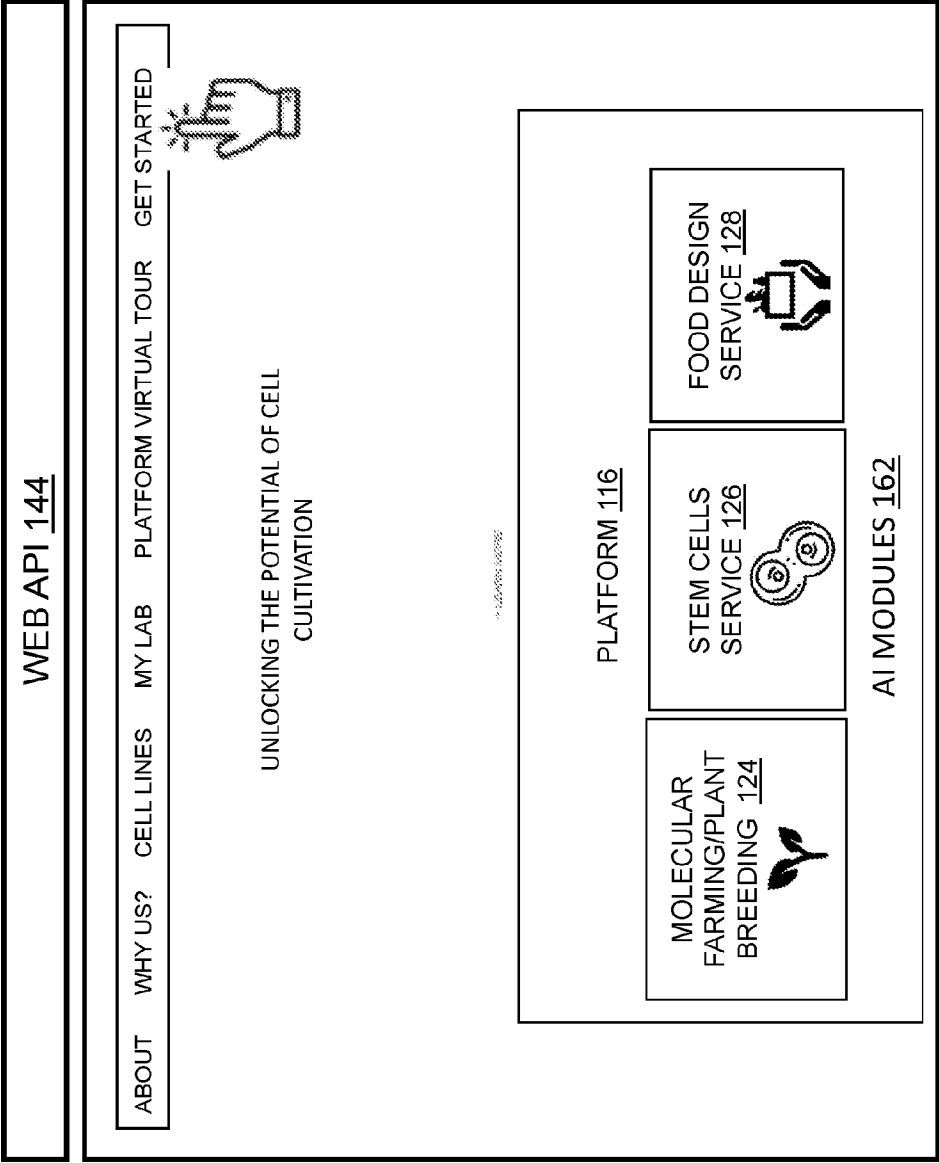


FIG. 5A

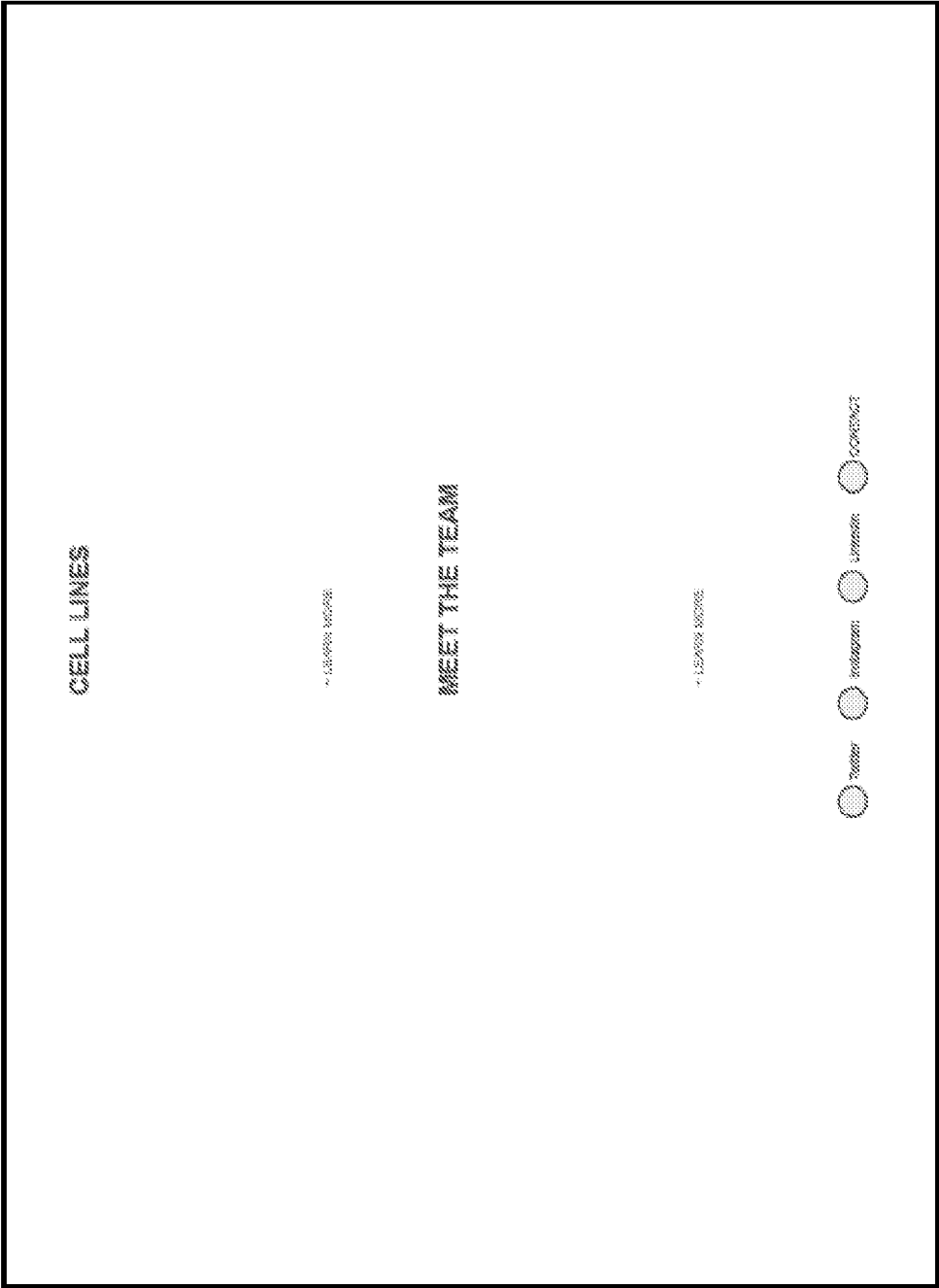


FIG. 5B

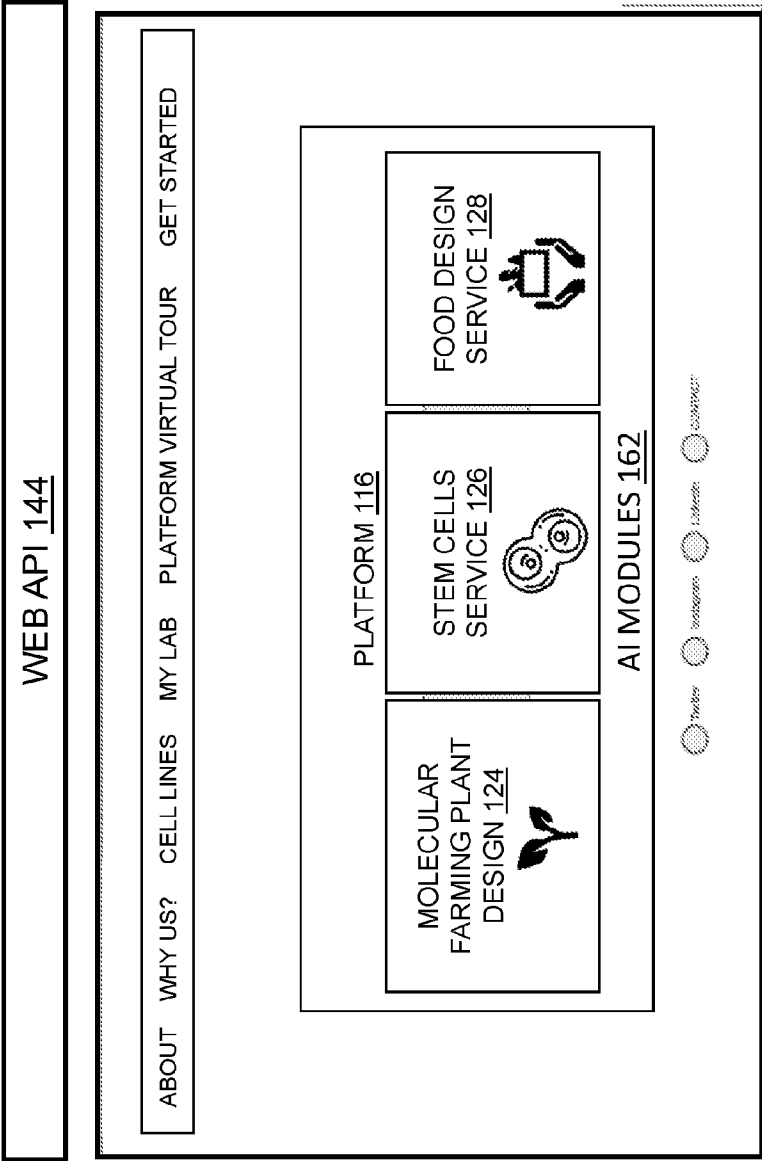


FIG. 6

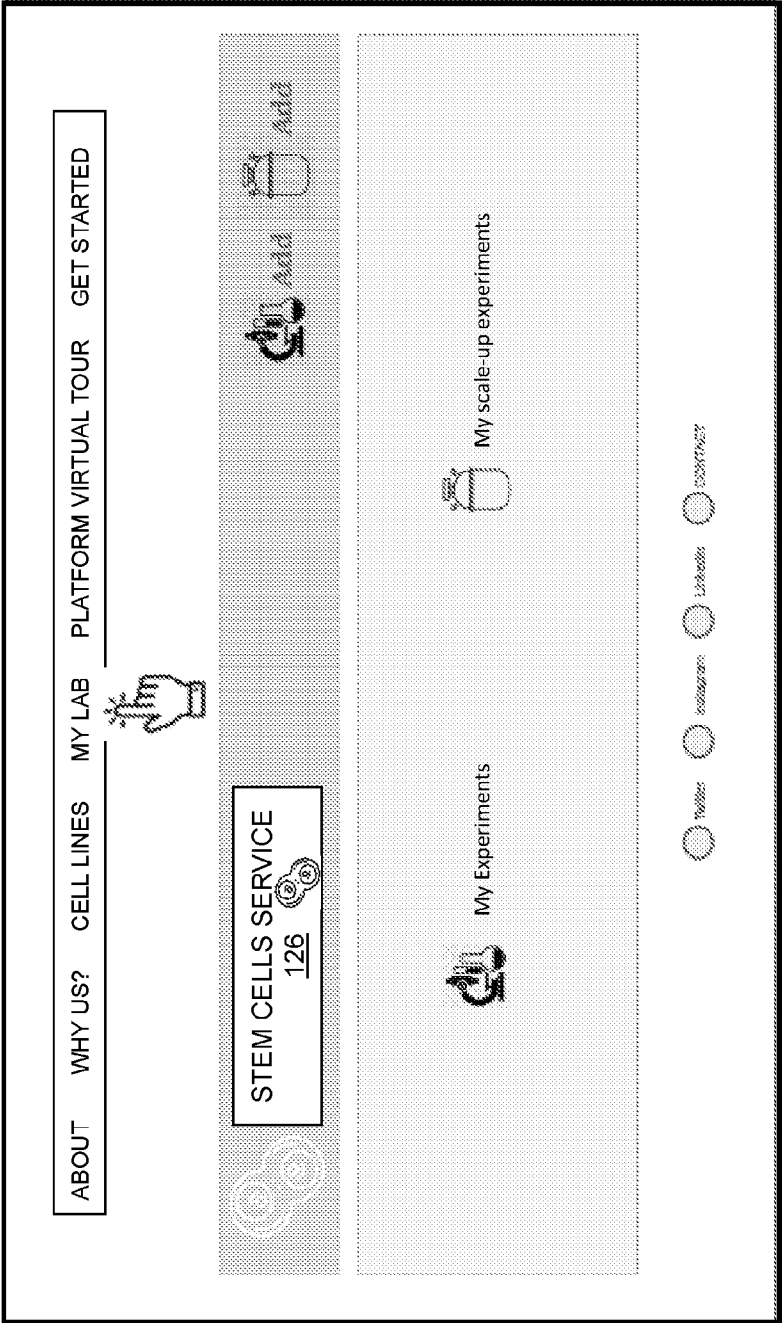


FIG. 7

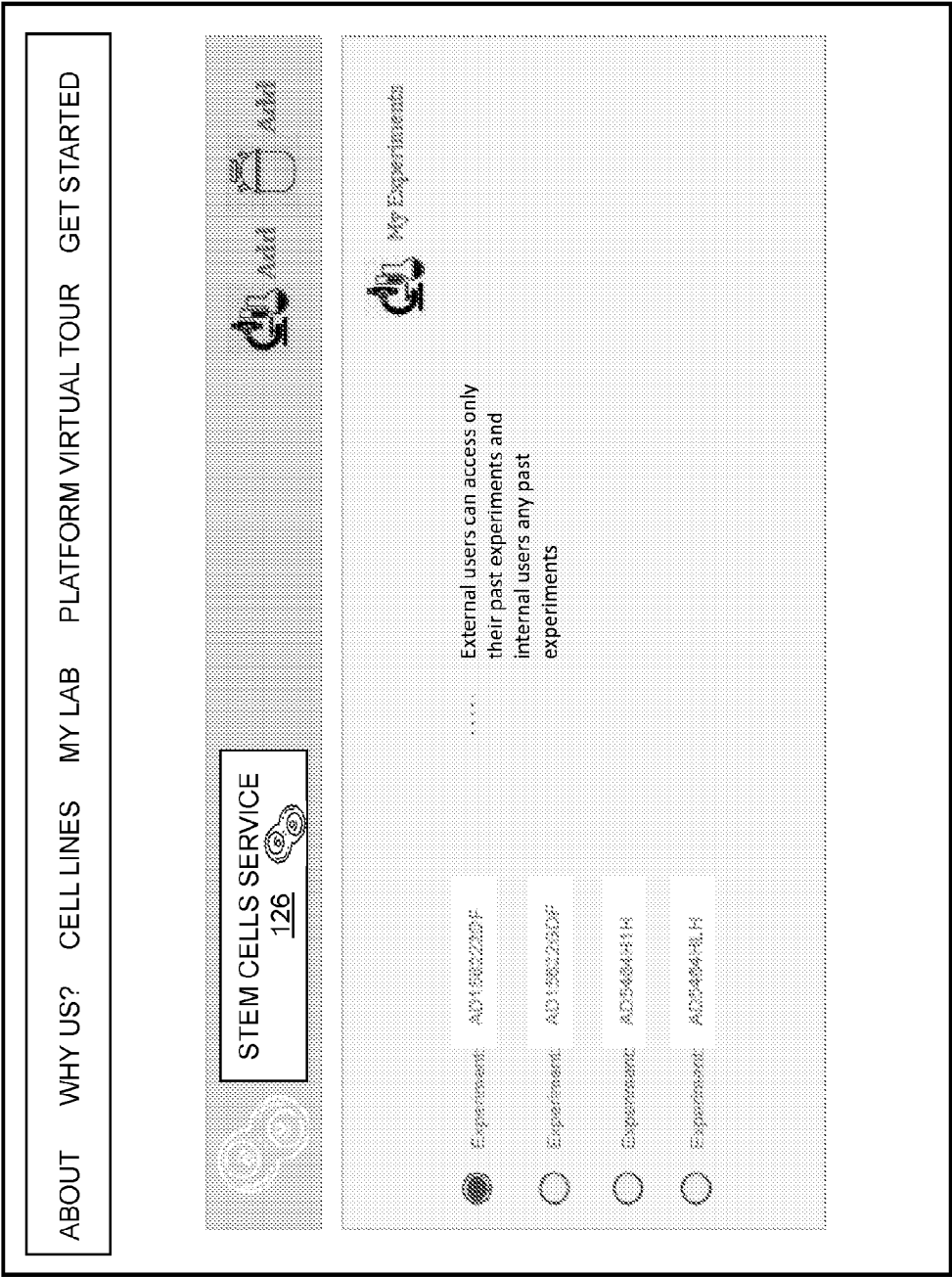


FIG. 8

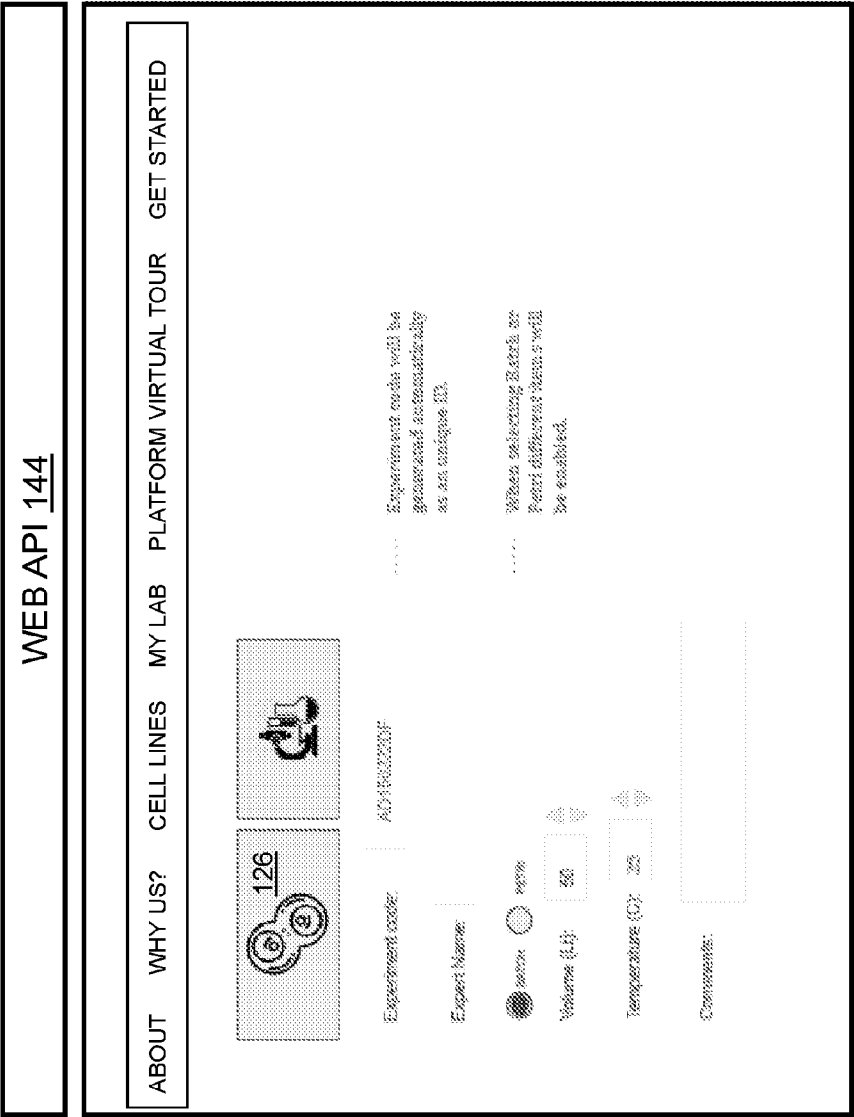


FIG. 9

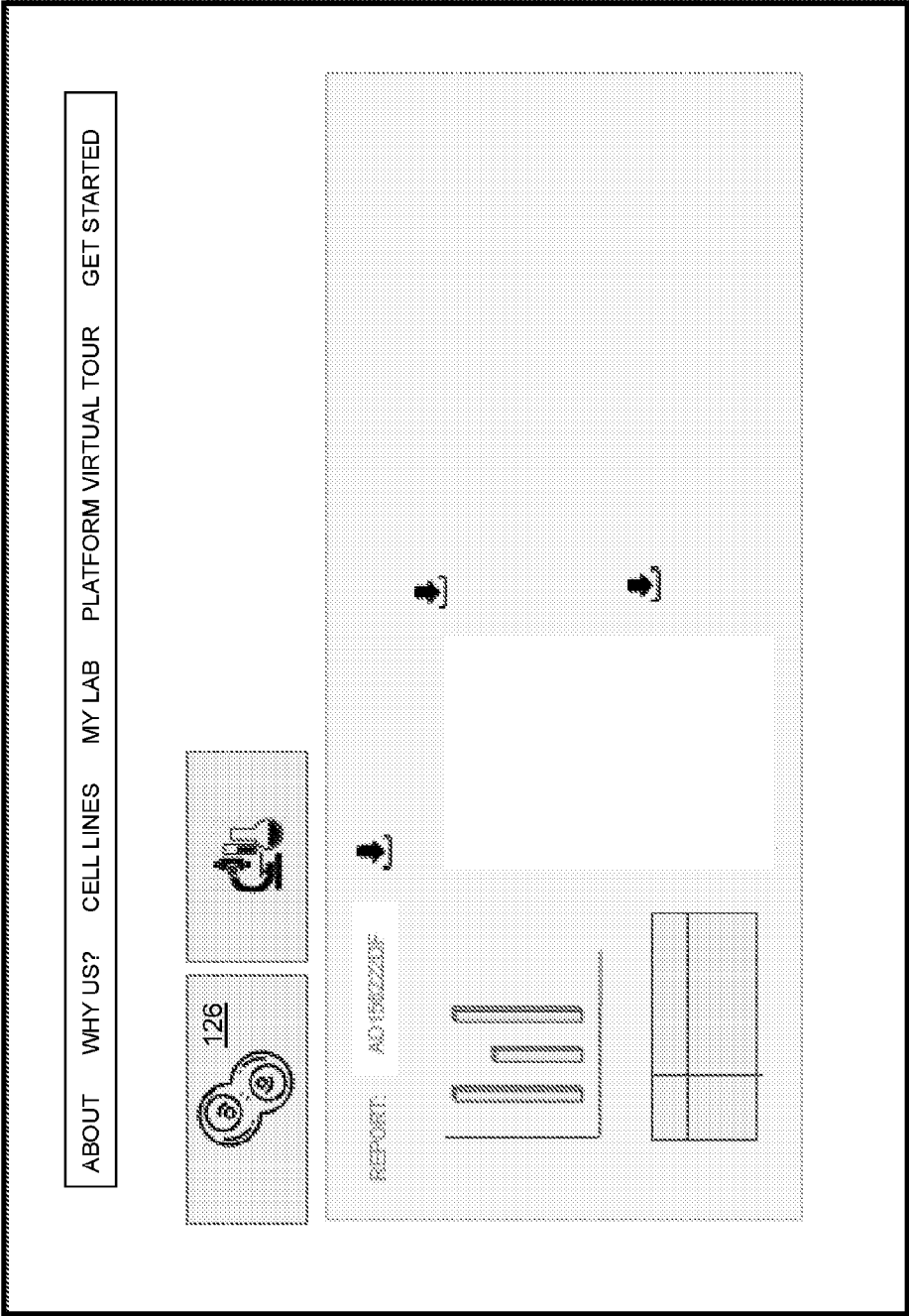


FIG. 10

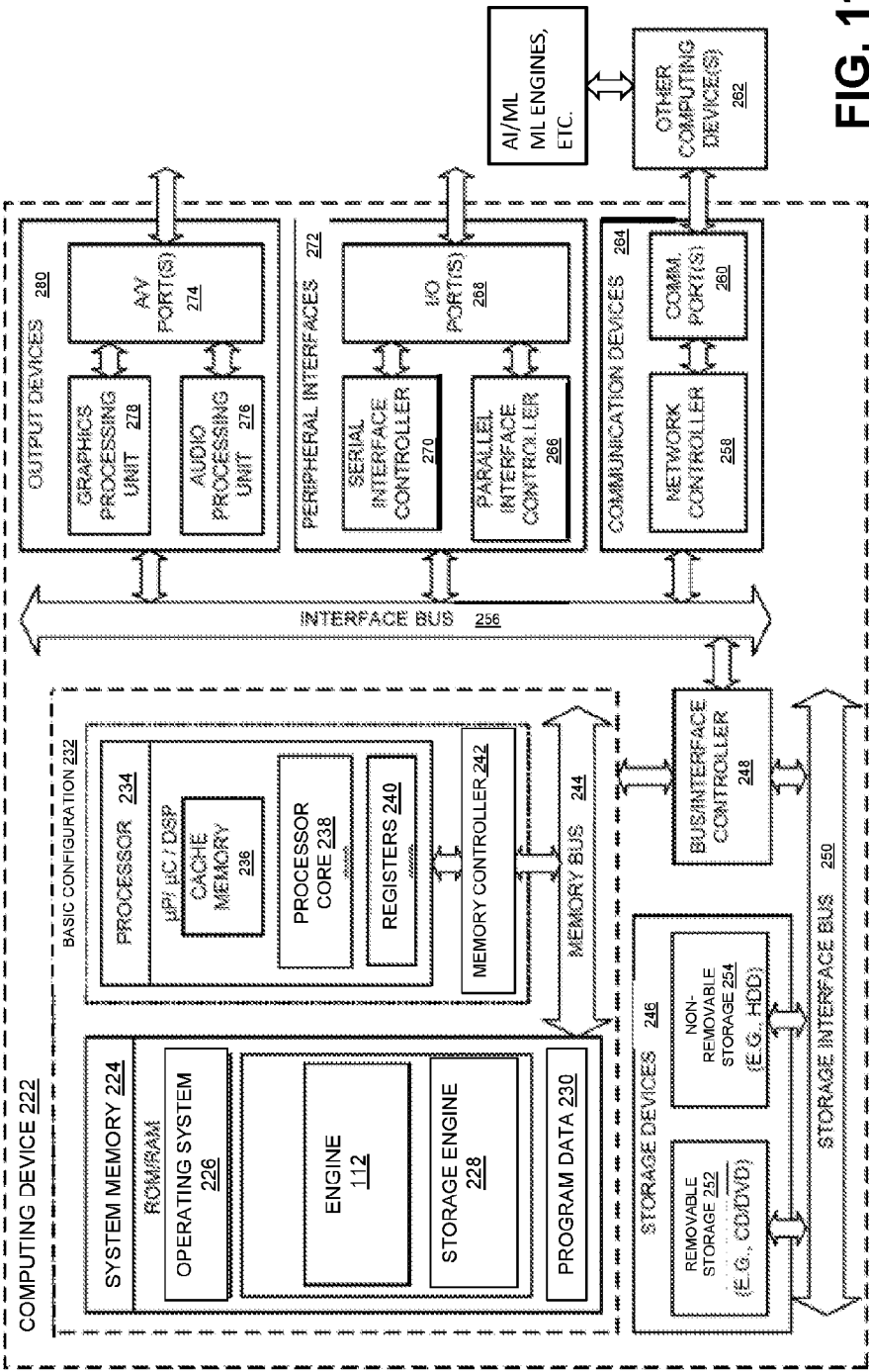


FIG. 11

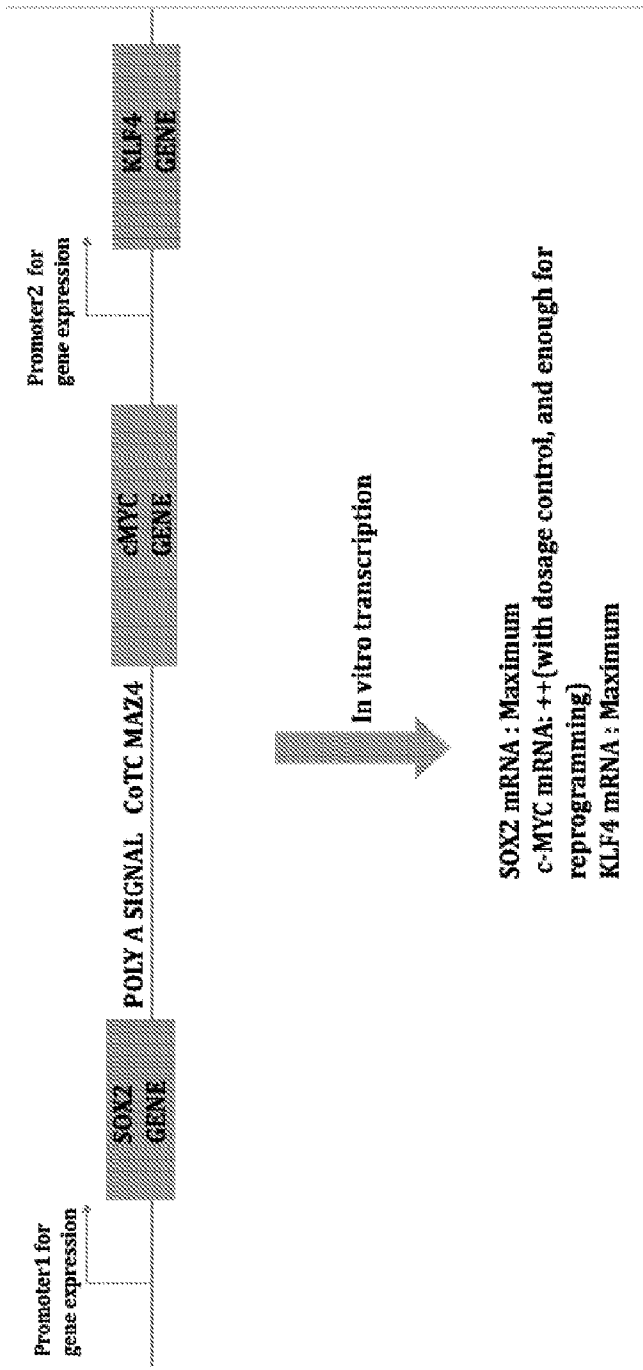


FIG. 12

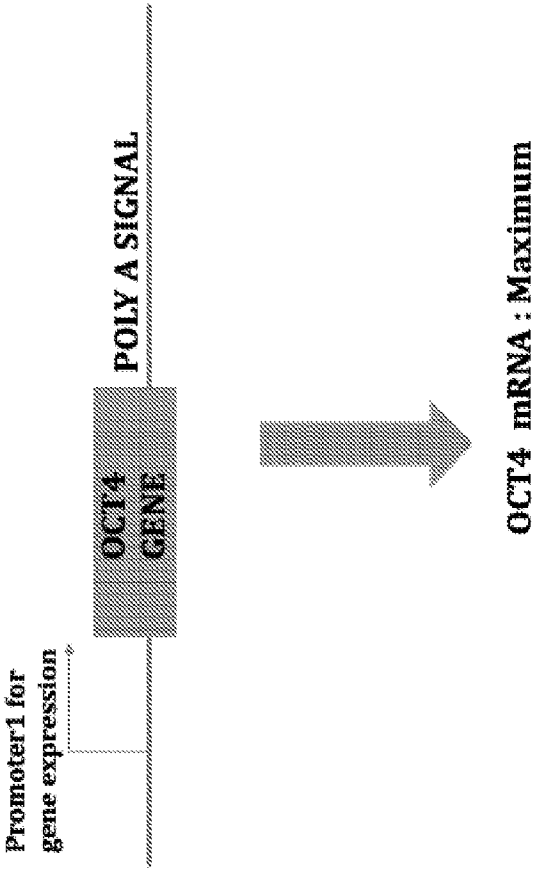


FIG. 13

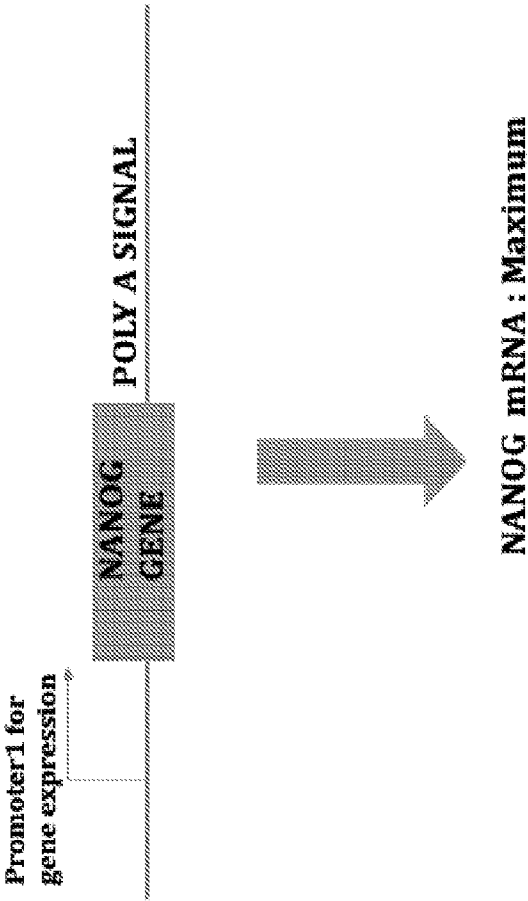


FIG. 14

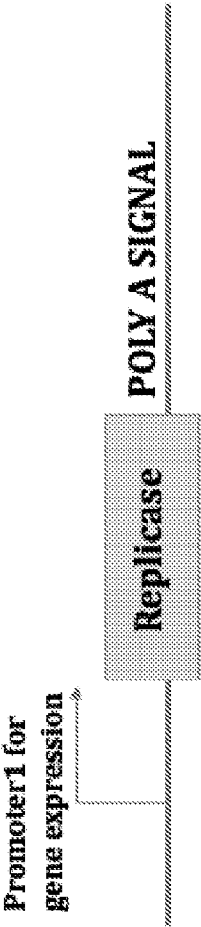


FIG. 15

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2023/055253

A. CLASSIFICATION OF SUBJECT MATTER INV. G06Q50/04 A01H4/00 C12M3/00 C12N1/00 C12N5/073 C12N15/00 G06N3/045 G16B5/00 G16B35/20 ADD. 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) A01H C12N C12M C12R G06F G06N G06Q G16B 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) EPO-Internal		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2021/090694 A1 (COLLEY SHANE [US] ET AL) 25 March 2021 (2021-03-25) paragraph [0947] paragraph [0964] paragraph [0973] – paragraph [0975] paragraph [0987] paragraph [1054] paragraph [1220] paragraph [1292] paragraph [1350] paragraph [1384] – paragraph [1385] paragraph [1733] figures 1, 11b, 12, 81, 184, 187A, 188, 192, 204 ----- -/--	1-23
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "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) "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 "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 "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 "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 "&" document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
18 August 2023		28/08/2023
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Hauber, Jörg

INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
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Information on patent family members

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