Health & Medicine

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Health & Medicine focuses on technical challenges relevant to the well-being of humans, non-human animals, and populations. Applications of engineering biology in this sector focus on preventing and eradicating disease and supporting longevity and quality of life. For related reading about tools and technologies that impact human and animal health, please see *Environmental Biotechnology* and *Food & Agriculture.*

Societal Challenge 1: Eradicate existing and emerging infectious diseases.

- Science/Engineering Aim 1: Mitigate the threat of microbial (non-viral) pathogens.
  - Engineering Biology Objective 1: Develop tools for rapidly and inexpensively diagnosing antimicrobial-resistant (AMR) susceptibilities and infections.
    - Gene Editing, Synthesis, and Assembly Achievement:
      - Error-free DNA synthesis for rapid, high-yield production of antibody proteins and sensors built from nucleic acids.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
      - Rapid antibody development for detecting AMR pathogens.
    - Host and Consortia Engineering Achievement:
      - Develop cell-free systems to detect RNA signatures of AMR pathogen susceptibility.
      - Improve properties such as shelf-life and levels of protein expression of cell-free systems.
      - Develop cell/tissue models to screen and test anti-AMR interventions *in situ*.
    - Data Integration, Modeling, and Automation Achievement:
      - Improve prediction of AMR-conferring operons and markers, and their risk of transmission between organisms, to inform diagnostic tools.
      - Models for transforming -omics data to levels of susceptibility and resistance.
      - Improve identification, prediction, and modeling of characteristic pathways leading to resistance (for example, sequences of genetic changes).
      - Automate electronic reader systems for cheap and fast sequencing of AMR markers and patient-susceptibility biomarkers.
  - Engineering Biology Objective 2: Develop tools to treat microbial infections, overcome antimicrobial-resistance, and reduce the dependence upon antibiotics in humans, pets, livestock, and other animal populations.
    - Gene Editing, Synthesis, and Assembly Achievement:
      - Gene delivery systems targeted to specific pathogens.
      - Scaled-up synthesis of high-quality DNA encoding anti-microbial gene circuits.

- Biomolecule, Pathway, and Circuit Engineering Achievement:
  - Develop evolvable therapies (for example, phage therapy that evolves with the microbes).
  - Rapid design and synthesis of customized, targeted therapeutics (including endonucleases, lysins, endopeptidases, and proteases) for inhibiting pathogenic cell growth.
- Host and Consortia Engineering Achievement:
  - Engineer a more diverse gut microbiome to prevent potential pathogenicity and increase resistance to gastrointestinal tract infections.
  - Engineer organisms that can be used to seed the gut microbiome for creating *in situ* antibiotic products.
  - Design of cellular features to support successful, non-toxic delivery and stabilization of living therapies in the patient.
- Data Integration, Modeling, and Automation Achievement:
  - Improve prediction of evolution of novel antimicrobial resistance-conferring mutations.
  - Improve design and prediction of targeted therapeutics.
  - Develop methods for optimization of treatment strategies that stop or prevent the evolution, emergence, and/or dominance of resistant subpopulations of bacteria.

- Engineering Biology Objective 3: Reduce transmission of disease to humans from non-human animals.
  - Gene Editing, Synthesis, and Assembly Achievement:
    - New tools for editing genes and pathways in insects and livestock that act as disease carriers and reservoirs.
  - Biomolecule, Pathway, and Circuit Engineering Achievement:
    - Development of additional, ultra-low-cost animal vaccines, and new vaccines for diseases not currently covered.
  - Host and Consortia Engineering Achievement:
    - Engineer cells of insects and animals that act as disease carriers and reservoirs to attenuate pathogenicity and/or neutralize the pathogen (Lane & Quistad, 1998).
  - Data Integration, Modeling, and Automation Achievement:
    - Develop better models to predict emergence and evolution of antibiotic resistance under complex scenarios.
- Engineering Biology Objective 4: Genetically encode disease resistance (such as in livestock).
  - Gene Editing, Synthesis, and Assembly Achievement:
    - Improve tools for genetic manipulation of animals.
  - Host and Consortia Engineering Achievement:
    - Engineer microbiomes to resist disease, such as through secretion of antimicrobial substances *in situ*.

- Engineer somatic cells for disease resistance; for example, by altering membrane components known to be points of attachment for certain pathogens, by enhancing immune memory to specific pathogens post-vaccine, or engineering chimeric antigen receptor (CAR) T cells for activity against fungal and other pathogens (Naran, Nundalall, Chetty, & Barth, 2018).

- Data Integration, Modeling, and Automation Achievement:
  - Computational identification of genes that confer disease resistance.

- Science/Engineering Aim 2: Diagnose and treat viral infections.
  - Engineering Biology Objective 1: Develop rapid, reliable diagnostics to detect viral infections.
    - Gene Editing, Synthesis, and Assembly Achievement:
      - Rapid, high-fidelity DNA synthesis for development and production of sensing technologies.
      - Gene editing technologies for building cell-based sensors.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
      - Sensitive and specific molecular sensing technologies, such as molecular probes or DNA amplification.
    - Host and Consortia Engineering Achievement:
      - Cell-expressed reporters for infection.
      - Synthetic epigenetic silencing of viral DNA.
    - Data Integration, Modeling, and Automation Achievement:
      - Point-of-care (POC) and/or microfluidic systems for automating patient sample preparation.
      - Cheap and fast sequencing of viral infection markers and patient susceptibility biomarkers.
  - Engineering Biology Objective 2: Develop tools to treat viral infections.
    - Gene Editing, Synthesis, and Assembly Achievement:
      - New gene editing tools to precisely neutralize or excise viral sequences from host genomes.
      - Scaled-up synthesis of high quality DNA encoding anti-viral gene circuits.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
      - Rapid design and synthesis of customized, targeted endonucleases for inhibiting viral replication.
    - Host and Consortia Engineering Achievement:
      - Synthetic epigenetic silencing of viral DNA.
      - Development of cell and tissue models to screen and test anti-viral interventions *in situ*.
    - Data Integration, Modeling, and Automation Achievement:
      - Systems biology approaches to identifying critical molecular weaknesses in viral function as drug targets.

        - Simulations to predict pace and breadth of epidemics and impact of molecular interventions.
- Science/Engineering Aim 3: Develop new and better vaccines, other prophylactic tools, and production pipelines.
    - Engineering Biology Objective 1: Design antigens and adjuvants that improve immune memory.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Rapidly produce antigen variants for validation.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - *De novo* development of synthetic immunogenic antigens.
        - Host and Consortia Engineering Achievement:
            - Better understanding of the heterogeneity of immune memory longevity for different pathogens and different individuals.
            - Ability to increase longevity of specific memory T and B cells.
        - Data Integration, Modeling, and Automation Achievement:
            - Modeling and prediction of the correlation between adjuvants and immune memory.
            - Modeling and prediction of how immune memory formation varies between individuals (with the inclusion of characteristics such as race, ethnicity, geography, and socioeconomic status) for different pathogens.
    - Engineering Biology Objective 2: Develop nucleic acid- and other biomolecule-based vaccines (including hybrid biologic/polymer-based vaccines).
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Automated, large-scale, combinatorial DNA assembly and screening to identify nucleic acid construct designs enabling robust antigen expression.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Low-cost nucleic acid synthesis.
            - Increase antigen expression through gene expression engineering.
            - Enable nucleic acid systems for robust expression of multiple antigens.
            - Improve vector design and delivery methods.
        - Host and Consortia Engineering Achievement:
            - Engineer cells to produce low-levels of antigen to promote longevity of memory immune responses *in vivo*, while minimizing host immune response against the engineered cells (Kedzierska, Valkenburg, Doherty, Davenport, & Venturi, 2012).
        - Data Integration, Modeling, and Automation Achievement:
            - Use analytics and modeling to identify transcriptional and translational regulatory elements enabling enhanced protein expression.

        - Deep-learning techniques for understanding “sequence grammar” of regulatory elements.
    - Engineering Biology Objective 3: Enable and advance the use of plants, cell cultures, and cell-free systems to produce vaccines.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Increase DNA synthesis and fidelity to build and characterize promoters, circuits, and pathways for antigen production.
            - Scaled up synthesis of DNA-based antigens.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Develop gene expression tools to increase vaccine (antigen) yield in non-animal expression systems.
        - Host and Consortia Engineering Achievement:
            - Engineer host cells and cell-free systems for high fidelity production of vaccines.
        - Data Integration, Modeling, and Automation Achievement:
            - Employ modeling and analytical approaches to identify critical factors affecting vaccine production and quality.
- Science/Engineering Aim 4: Develop better population-scale surveillance methods for emerging infectious diseases and create technologies to rapidly address outbreaks and epidemics in real time.
    - Engineering Biology Objective 1: Advance engineering of biological tools to detect and track pathogen reservoirs and flow over time and space.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - DNA-based event recording (DNA barcoding).
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Development of simple and cheap, biomolecule-based kits for surveillance and analysis.
        - Host and Consortia Engineering Achievement:
            - Next-generation live cell reporting systems.
        - Data Integration, Modeling, and Automation Achievement:
            - Advanced models for pathogen flow through the environment and populations in real time.
    - Engineering Biology Objective 2: Develop tools to rapidly characterize and respond to known and unknown pathogens in real time at population scales.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Diagnostics for nucleic acids indicative of the presence of specific pathogens, utilizing targeted DNA- and RNA-binding Cas editors.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Development of strain-specific vaccines in real time (i.e., during an outbreak).
        - Host and Consortia Engineering Achievement:
            - Engineer microbes that detect pathogenic antigens and react by secreting anti-pathogen factors.

        - Data Integration, Modeling, and Automation Achievement:
            - Advanced bioinformatics to quickly characterize emerging pathogens from genetic sequences and epigenetic markers.

Societal Challenge 2: Address non-communicable diseases and disorders. Regarding non-communicable diseases and disorders, we consider the advancement engineering biology tools and technologies to address cancer, addiction, obesity, neurodegenerative diseases, aging-related disorders, psychiatric disorders, heart disease, diabetes, and other genetic disorders and lifestyle diseases.

- Science/Engineering Aim 1: Measure molecular markers of disease.
    - Engineering Biology Objective 1: Develop biosensors for measuring metabolites, proteins, and other biomolecules *in vivo*.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - High-fidelity production of complex large, functional DNAs and RNAs (such as aptamers and riboswitches).
            - Efficient production of >1 kilobase biosensor genes and circuits that may contain repeat elements for sensing multiple input signals.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Identify biosensors for molecules for which there are currently no biosensors.
            - Identify fast and reliable biosensor readouts for *in vivo* applications.
            - Engineer memory circuits to record the presence of metabolites and proteins and the intensity and duration of those signals.
        - Host and Consortia Engineering:
            - Enable selective transfection/transduction and delivery of large biosensor sequences and circuits into host cells.
        - Data Integration, Modeling, and Automation Achievement:
            - Genome mining for biosensors.
            - Identify design principles to incorporate these biosensors into different hosts.
            - Leverage machine learning technologies to facilitate deconvolution and identification of biosensor signals.
- Science/Engineering Aim 2: Generate new drug therapies.
    - Engineering Biology Objective 1: Develop platforms for rapidly and effectively identifying drugs to treat non-infectious diseases.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Rapid and cost efficient synthesis of genetic circuits.
            - Parallel and error-free genome engineering of mammalian cell lines.

        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Development of novel, high-affinity agents, such as antibody proteins, nucleic acids, and other macromolecules, that bind drug targets.
            - Macromolecular adducts (chemical “tags”) to control the distribution and delivery of drugs within cells, tissues, and organs.
            - Novel modulators of cell pathways that show little or no off-target toxicity.
        - Host and Consortia Engineering Achievement:
            - Genetically-encoded reporters for real-time tracking of drug activity in cells, tissues, and microbiomes.
            - Microbial reporters to detect gastrointestinal tract cell stress signals.
        - Data Integration, Modeling, and Automation Achievement:
            - Develop automated, large-scale screening platforms for drug discovery.
            - Powerful associative analyses to link gene and protein networks to disease states.
            - Models to predict biased accumulation of drug in certain tissues based on the chemical and/or physical properties of the drug.
            - Drug-to-disease database and associated software/informatics tools to rapidly evaluate potential for drug repurposing.
    - Engineering Biology Objective 2: Identify patient-specific drugs.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Identify patient-specific genetic biomarkers.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Artificial co-evolution of macromolecular therapeutics which change in response to a patient’s unique biochemistry.
            - Anticipatory library of therapeutic variants that contain best-matches for patient-specific drug target variants.
        - Host and Consortia Engineering Achievement:
            - Development of patient-matched disease models (such as organoids).
        - Data Integration, Modeling, and Automation Achievement:
            - Develop libraries of drug efficacy correlated to de-identified patient biomarkers, used to identify promising patient-specific drugs.
            - Use modeling and bioinformatics to predict novel interventions on an individualized basis.
- Science/Engineering Aim 3: Develop and hone genetic engineering/gene therapies.
    - Engineering Biology Objective 1: Develop targeted delivery of gene therapies to specific tissues and cells.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Rapid and cost-efficient synthesis of genetic circuits.

        - Efficient DNA editing in mitochondria.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
        - Non-immunogenic macromolecules and vesicles to deliver therapeutic DNA, RNA, and proteins to cells and tissues.
    - Host and Consortia Engineering Achievement:
        - Increase the payload size for DNA delivery vectors by at least ten-fold.
        - Produce optimal epigenetic imprinting patterns in induced pluripotent stem cells (iPSC) and artificially-differentiated cells.
    - Data Integration, Modeling, and Automation Achievement:
        - Generate models to predict efficiency of DNA/RNA delivery based on the structure of the payload and features of the target cell or tissue.
- Engineering Biology Objective 2: Regulate, control, and maintain gene therapies.
    - Gene Editing, Synthesis, and Assembly Achievement:
        - Rapid and cost efficient synthesis of genetic circuits.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
        - Circuits that enable temporal control of gene therapy localization and activation.
    - Host and Consortia Engineering Achievement:
        - Prevent immune system from reacting to or eliminating gene therapy.
    - Data Integration, Modeling, and Automation Achievement:
        - Develop predictive models to determine optimal maintenance/scheduling of gene therapies.
        - Automation to rapidly design, build, and test circuit designs in mammalian cells.

- Science/Engineering Aim 4: Advance engineered cell systems (including the human microbiome and immune system), organs, and tissues to manage and treat disease and disease outcomes.
    - Engineering Biology Objective 1: Characterize, engineer, and manipulate different microbiota throughout the body for health purposes.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Re-code microbial genomes/chromosomes.
            - Targeted gene editing systems for specific microbes or cell types.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Engineer enzymes to enhance or alter metabolism.
            - Engineer secretion systems for *in vivo* delivery of therapeutics from microbes.
        - Host and Consortia Engineering Achievement:
            - Rationally design and engineer microbial cells and communities.

        - Achieve short- and long-term, predictable tuning of the microbiome to deliver therapeutics, add functions and enzymes, and remove organisms.
    - Data Integration, Modeling, and Automation Achievement:
        - Advanced modeling of interactions between microbes within the microbiota and their host.
        - Ecological models that incorporate changes in host, microbes, and the local environment (more specifically, the location in gastrointestinal tract, in the skin, etc.), and enable prediction of therapeutic approach.
        - Develop models that focus on function (enzymes, pathways) to diagnose and predict dysbiosis.
        - Employ statistically rigorous models to differentiate correlation and causation with respect to changes in the microbiome, as correlations are still valuable for diagnostics but therapies and interventions should be focused where there is a causative or clearly functional link.
- Engineering Biology Objective 2: Create cell-autonomous genetic circuits to drive tissue formation and repair.
    - Gene Editing, Synthesis, and Assembly Achievement:
        - Achieve stable expression from synthetic transgenes.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
        - Engineer macromolecules with predictable, robust, orthogonal dynamic behavior that demonstrate no unintended cross-interaction with other factors.
        - Engineer libraries of synthetic, orthogonal cell-communication mechanisms, including short-range communication (receptors) and long-range communication (morphogens).
    - Host and Consortia Engineering Achievement:
        - Engineer mechanisms to coordinate behavior of single cells in a population and interaction with the host (i.e., patient).
        - Customize the function and number of major cellular features, including cell surface proteins, the cytoskeleton, organelles, and chromosomes.
    - Data Integration, Modeling, and Automation Achievement:
        - Rapid single-cell -omics pipelines to understand the molecular and cellular recipes in development and tissue formation.
- Engineering Biology Objective 3: Engineer immune cell-based therapies.
    - Gene Editing, Synthesis, and Assembly Achievement:
        - Improve parallel and precise genome editing in primary immune cells.

- Biomolecule, Pathway, and Circuit Engineering Achievement:
  - Improve biosensor and genetic circuit designs to improve specificity, efficacy, and safety.
- Host and Consortia Engineering Achievement:
  - Engineer mechanisms to coordinate behavior of single cells and their interaction with the human host.
- Data Integration, Modeling, and Automation Achievement:
  - Increase the reliability of predicting protein, pathway, and circuit function from sequences to enable better biosensor, receptor, and genetic circuit designs.

- Engineering Biology Objective 4: Enable biocompatible allo- and xeno-transplant and implantation of synthetic or engineered (including "printed") tissues/organs.
  - Gene Editing, Synthesis, and Assembly Achievement:
    - Improve parallel and precise genome editing in recipient's immune system to establish or increase tolerance to the donor tissue/organs and immunize against cross-species disease transmission.
    - Improve parallel and precise genome editing in donor animals to reduce or remove immunogenicity and cross-species disease transmission.
  - Biomolecule, Pathway, and Circuit Engineering Achievement:
    - Develop biosensors for identifying xenoreactive immune cells.
    - Engineer libraries of synthetic, orthogonal cell-communication mechanisms, including short-range communication (receptors) and long-range communication (morphogens).
    - Enable production of synthetic and engineered bioscaffolds for tissue regeneration.
  - Host and Consortia Engineering Achievement:
    - Engineer the recipient's immune system to be specifically tolerant of the implant without excessive immune suppression.
  - Data Integration, Modeling, and Automation Achievement:
    - Advanced modeling of interactions between implant/transplant and the host.
    - Rapid single-cell -omics pipelines to understand the molecular and cellular characteristics of development and tissue formation.

Societal Challenge 3: Address environmental threats to health, including toxins, pollution, accidents, radiation, exposure, and injury.

- Science/Engineering Aim 1: Integrate (bio)materials and living tissues to address injuries and navigate dangerous environments.
    - Engineering Biology Objective 1: Enable greater and more beneficial interaction of living cells and tissues with prosthetics.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Parallel, scalable, and cost-effective genome engineering to enable the use of allogeneic cell sources, as opposed to patient-specific sources.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Develop and rapidly produce biomolecule-based materials (biomaterials) that have improved physiological properties.
            - Develop biopolymers with physical durability to resist long-term wear and tear.
            - Achieve minimally-invasive control of synthetic gene and protein networks with light-programmable macromolecules (advanced optogenetics).
        - Host and Consortia Engineering Achievement:
            - Engineer cellular pathways, extracellular matrices, and connective tissues that enhance prosthetic compatibility without compromising health.
        - Data Integration, Modeling, and Automation Achievement:
            - Identify predictive, detectable, micro-scale biosignatures (biological outputs) that correlate with health, damage, or disease.
    - Engineering Biology Objective 2: Integrate wearable tech with living cells to sense and act upon threats to health.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Develop systems for reliable genomic integration of reporters that will sense specific cell states in high-risk populations, where the molecules/states can be sensed, analyzed, and acted upon externally (electronic or optic signaling).
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Develop sensing and reporting systems that enable *in situ* detection of toxins and disease indicators, where the info can be sensed, analyzed, and acted upon externally (electronic or optic signaling) or in a more integrated fashion.
        - Host Engineering Achievement:
            - Develop probiotics and similar cell systems that can report to external devices.
            - Tune select cells or tissues to interact with stimuli from external (electronic) devices in a highly controlled manner.

        - Data Integration, Modeling, and Automation Achievement:
            - Develop and advance modeling and analytics to integrate information from wearable tech, medical sensors (like those for continuous glucose monitoring), and eventually *in vivo* sensors, to predict health, physical performance, toxin exposure, disease, other states of interest.
            - Use novel machine learning approaches to integrate different types of sensor data and address variation between people and populations.
            - Design and model systems that both sense and act upon threats, with reliable communication and data integration.
            - Expand and improve algorithms for estimating health states based on a limited set of measurable data.
    - Engineering Biology Objective 3: Engineer the immune system to improve allotransplant of tissues, organs, and limbs.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Achieve highly efficient, rapid genetic or epigenetic editing of the allograft genome with synthetic gene cassettes or whole chromosomes.
            - Achieve efficient co-editing of human leukocyte antigen (HLA) gene clusters to prevent allograft rejection.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Generate potent gene delivery vehicles for immune gene clusters (such as HLAs) and whole synthetic chromosomes.
            - Develop macromolecules to neutralize or mask non-self protein markers.
        - Host and Consortia Engineering Achievement:
            - Remove potent non-self antigens from allograft tissues/organs.
            - Replace non-self with “self” markers in allograft cells.
        - Data Integration, Modeling, and Automation Achievement:
            - Achieve data-driven molecular profiling of key antigens to identify engineerable donor tissue and support patient-to-allograft matching.
- Science/Engineering Aim 2: Develop systems to detect, identify, reverse, neutralize, and clear biochemical damage.
    - Engineering Biology Objective 1: Prevent, reverse, or neutralize microlesions induced by toxins, radiation, and other factors.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - High-fidelity production and delivery of DNA and non-coding RNAs to aid DNA damage repair.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Design robust, mutation-specific, base-editors.

        - Deliver synthetic repair machinery into the nucleus and mitochondria.
        - Design lipids and cell surface features to reverse cell membrane damage.
    - Host and Consortia Engineering Achievement:
        - Induce prophylactic genetic and epigenetic states in somatic cells prior to exposure (an interesting example of this might be conditioning astronauts for space exploration).
    - Data Integration, Modeling, and Automation Achievement:
        - Use data analytics and modeling to predict microlesion weak-spots (e.g., DNA, RNA, protein hotspots) to support anticipatory medical care.
- Engineering Biology Objective 2: Neutralization and clearance of toxic substances from the body.
    - Gene Editing, Synthesis, and Assembly Achievement:
        - Achieve highly-efficient, rapid gene editing to enable cells to detect and neutralize threats as needed.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
        - Develop biomolecular reporters to track migration and accumulation of toxins through the body.
        - Generate macromolecules that neutralize and clear prions and protein plaques from the body.
        - Design high-affinity molecules to bind and clear toxins from the body (an interesting example of this might be a synthetic antivenom).
    - Host and Consortia Engineering Achievement:
        - Generate and engineer hosts and cell-free systems that can act as bio-factories to produce anti-toxins at practical scales.
    - Data Integration, Modeling, and Automation Achievement:
        - Models to predict symptoms, onset, and timing of poisoning, to inform the rational design of antidotes and treatment regimes.

Societal Challenge 4: Promote equitable access to healthcare, patient representation in research, democratization of medicine, and the development of personalized medicines.

- Science/Engineering Aim 1: Develop patient-specific testbeds for drug treatments to support patient representation and personalized medicine.
    - Engineering Biology Objective 1: Develop induced pluripotent stem cell (iPSC)-derived organoids as personalized models.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Deliver and stabilize the expression of synthetic DNA in iPSCs.
            - Use nucleases to efficiently edit very small numbers of cells with minimal error.

        - Identify and characterize differences in gene expression profiles between human primary tissues and iPSC-derived tissues.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
        - Develop nanocarriers to efficiently deliver macromolecules into small numbers of cells.
    - Host and Consortia Engineering Achievement:
        - Develop patient-specific organ-on-a-chip devices to model individual patient response to drug treatments across organ systems.
        - Develop minimally-invasive methods to collect and culture useful cells.
    - Data Integration, Modeling, and Automation Achievement:
        - Establish databases of genetic and metabolic expression and activity profiles of iPSCs and iPSC-derived tissues.
- Engineering Biology Objective 2: Personalize medical treatments to human subpopulations and/or individuals. (Dehingia, Adak, & Khan, 2019; Hooker et al., 2019; Molteni, 2019)
    - Gene Editing, Synthesis, and Assembly Achievement:
        - Develop fast, high-fidelity, on-demand synthesis of large fragments of customized DNA and RNA for clinical use.
    - Biomolecule, Pathway, and Circuit Engineering Achievement:
        - Develop macromolecules and gene circuits that sense and report the local cellular or tissue environment.
    - Host and Consortia Engineering Achievement:
        - Develop living therapeutic cells that switch phenotypes in response to the local tissue environment.
        - Develop allergen-free platforms and cells for drug production.
    - Data Integration, Modeling, and Automation Achievement:
        - Model variants and alleles present in the human population to better understand and mitigate health challenges.
        - Identify useful semi-generalizable (familial or population-wide) features to help accelerate diagnoses and the design of treatment regimes.

- Science/Engineering Aim 2: Make cutting-edge therapy more available and affordable.
    - Engineering Biology Objective 1: Scale-up hard-to-produce therapeutic molecules, proteins, and cell therapies.
        - Gene Editing, Synthesis, and Assembly Achievement:
            - Parallel, scalable, and cost-effective genome engineering to enable the use of allogeneic cell sources, as opposed to patient-specific sources.
        - Biomolecule, Pathway, and Circuit Engineering Achievement:
            - Engineer temperature-stable, active macromolecule- and cell-based therapies.

- Design molecular features to support inexpensive, robust purification and processing of therapeutics.
- Develop circuits that behave robustly across different growth media.

- Host and Consortia Engineering Achievement:
  - Develop and characterize select microbes for advanced-therapeutics production in stationary phase.
- Data Integration, Modeling, and Automation Achievement:
  - Create publicly-accessible and encrypted databases of health-related data.
  - Identify critical metabolic/molecular bottlenecks and work-arounds for hard-to-produce therapeutics.

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