Attachment 1: Glossary and References

Complement-ARIE (Complement Animal Research In Experimentation) Challenge

Glossary:

For the purposes of this prize competition, the NIH Common Fund is focusing on the following areas of human-based NAMs: 1) complex *in vitro* cell- or tissue-based models; 2) *in silico* modeling and simulations; 3) *in chemico* cell-free systems; and 4) combination and integration of *in vitro*, *in silico* and *in chemico* approaches to include corresponding datasets addressing the FAIR (Findability, Accessibility, Interoperability, and Reusability) principles and enabling the use of AI/ML to generate testable predictions and risk assessments.

- *In vitro* models: three-dimensional (3D) human-derived tissue or cell culture technologies that more closely resemble *in vivo* cell environments that may include use of spheroids, organoids, bioprinted constructs, tissues/organs-on-chips or microphysiological systems.
- *In silico*: computational models that incorporate biological data with mathematical and computer-based representations to construct models of human biology using methods such as data analyses, data mining, homology models, machine learning, pharmacophores, quantitative structure-activity relationships, and network analysis tools.
- *In chemico*: cell-free systems that can recapitulate, probe, or augment normal cellular, tissue, or organismal processes, for example, reactive abiotic chemical methods that test the properties of substances, recombinant artificial membranes to model metabolite or drug transport, or synthetic biology approaches to produce macromolecules with more human-like post-translational modifications.
- FAIR: findable, accessible, interoperable, reusable data.
 - Findable: For data to be findable there must be sufficient metadata; there must be a unique and persistent identifier; and the data must be registered or indexed in a searchable resource.
 - o Accessible: To be accessible, metadata and data should be readable by humans and by machines, and it must reside in a trusted repository.
 - o Interoperable: Data must share a common structure, and metadata must use recognized, formal terminologies for description.
 - o Reusable: Data and collections must have clear usage licenses and clear provenance, and meet relevant community standards for the domain.
- **Precision medicine**: also known as "personalized medicine" is an innovative approach to tailoring risk assessment, diagnosis, and disease prevention and treatment based on an individual's genetics, environment, lifestyle, age, and diet/nutrition. It aims to provide the right treatment for the right patient at the right time, considering these factors.

References

Alon, Uri. An Introduction to Systems Biology: Design Principles of Biological Circuits. CRC Press, 2007.

Baker, Monya. "Reproducibility: Check your Chemistry." Nature, vol. 548, no. 7668, 2017, pp. 485-488.

Barh, Debmalya, et al. "In silico disease model: from simple networks to complex diseases." NCBI, www.ncbi.nlm.nih.gov/pmc/articles/PMC7325851/.

Clevers, H. "Modeling Development and Disease with Organoids." Cell, vol. 165, no. 7, 16 June 2016, pp. 1586-1597, doi:10.1016/j.cell.2016.05.082.

Flach, Erik H., et al. "Limitations of Quantitative Genetic Analysis: The Role of Environmental Effects." PLoS One, vol. 8, no. 5, 2013, e61707.

Kitano, Hiroaki. "Systems Biology: A Brief Overview." Science, vol. 295, no. 5560, 2002, pp. 1662-1664.

Noble, Denis. "Modeling the Heart—from Genes to Cells to the Whole Organ." Science, vol. 295, no. 5560, 2002, pp. 1678-1682.

Virumbrales-Muñoz, María, and Jose M. Ayuso. "From microfluidics to microphysiological systems: Past, present, and future." Organs-on-a-Chip, vol. 4, 2022, p. 100015, doi:10.1016/j.ooc.2022.100015.