Highlight report from mSBW 2025

The 2025 International Mammalian Synthetic Biology Workshop, held at UC Irvine, brought together researchers working at the forefront of mammalian cell engineering. Across multiple sessions, speakers highlighted advances in, among others, therapeutic applications and bioproduction, underscoring biological tools are now shaping translational pipelines.

On the bioproduction side, **Carlos Llanos (UCL)** presented an excellent overview of how synthetic biology approaches can be leveraged to address the unfolded protein response (UPR)**,** a longstanding bottleneck in industrial cell culture. In recombinant protein production, high expression loads often overwhelm the endoplasmic reticulum, triggering stress responses that reduce yields and impact product quality. Llanos discussed strategies to decouple productivity from stress induction, including engineering adaptive stress-response pathways and rewiring transcriptional regulators to improve folding capacity. This work aimed to tackle one of the longstanding issues of biomanufacturing community, using shCHOP and XBP1s based genetic feedback circuits and showing improved monoclonal antibody production.

Another highlight was the talk from **Katie Galloway (MIT)**, who focused on modular approaches to programming mammalian cells. She demonstrated how gene circuits are largely dependent on the transcriptional unit syntax (in tandem, convergent or divergent), a concept highly relevant not only to therapeutic circuits but also to bioproduction control. By showing case studies where cells could be tuned to balance growth and productivity dynamically, her work highlighted a future where bioprocesses may increasingly rely on pre-programmed genetic logic rather than external feeding strategies. This blending of synthetic biology design principles with process engineering showed a simple yet effective way to re-think our genetic circuit designs.

Although the conference had a strong emphasis on therapeutic applications, particularly in immuno-oncology, two talks stood out for showing how broadly applicable mammalian synthetic biology has become. **Michael Elowitz (Caltech)**, a pioneer in the field, described pyroptosis as an alternative effector mechanism to apoptosis in engineered kill switches. This was framed in the context of cancer immunotherapy but also carried lessons for anyone designing circuits with cell-fate outcomes. He also mentioned “polytransfection scans,” a powerful methodology to explore the combinatorial space of plasmid concentrations and stoichiometries. While directly relevant to dCas-based effector systems, the underlying principle — high-throughput, quantitative mapping of design space — has clear implications for improving experimental workflows across mammalian systems.

Wendell Lim (UCSF) provided a forward-looking perspective on the next stage of mammalian synthetic biology. He emphasized that while the field has generated individual “commands” — circuits for expression control, proliferation, or killing — the next challenge is to integrate these into higher-order programs that can perform in complex tissue environments. His example of a “brain GPS” circuit for glioblastoma, based on BCAN-specific targeting, reinforced the broader theme of the meeting: that mammalian synthetic biology is now mature enough to tackle multi-layered problems, from clinical translation to industrial bioproduction. This was showcased as well by **Tim Lu (Senti Bio),** who showed how Senti Bio is using highly engineered CAR-T cells that contain three independent circuits as a NOR gate, aiming for high specificity against cancer cells, in a field where, as he suggested, specificity and efficiency are correlated.

Attending the conference was made possible thanks to funding from ESACT-UK**,** whose support enabled me to engage directly with the community and bring back insights that will influence my own work and, hopefully, my colleagues'. Their investment in fostering participation underscores the importance of keeping bioproduction perspectives represented in broader synthetic biology discussions, as the tools the field is constantly formulating and evolving are already empowering the world of bioproduction.