

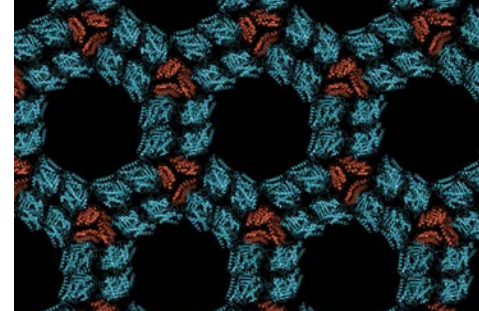
# From fundamental research to the development of new tools

Scientific breakthroughs are often based on technological and methodological breakthroughs. As a leading fundamental research institute, the I2BC is at the forefront of technological progress, developing innovative scientific methodologies, tools and approaches.

At I2BC, researchers study integrative cell biology, exploring various scales ranging from single molecules to entire organisms. With our wide range of know-how and expertise, we have developed innovative technologies and tools with numerous applications across multiple industries, ranging from agricultural to pharmaceutical fields.



# From fundamental research to the development of new tools



- **alphaReps:** we have generated **alternative antibody tools** capable of targeting proteins by designing large synthetic libraries of folded and soluble small single-chain proteins with randomized binding surfaces. This breakthrough enables cost-effective production of novel protein binders, specifically tailored to target proteins of interest, as selected through phage-display techniques<sup>1</sup>
- **New peptides and proteins:** we have developed techniques to synthesize peptides and proteins containing an almost infinite range of non-canonical amino acids. This is achieved using purified prokaryotic cell-free systems and flexizyme-acylated tRNAs<sup>2</sup>
- **Recombinant viral glycoprotein:** our expertise allows for the modification of viral glycoproteins, altering the tropism to target specific cells of interest. This opens up opportunities for precise targeting of G proteins to receptors of interest, such as tumor antigens, and holds potential for gene therapy and oncolytic applications<sup>3</sup>
- **Probing redox processes for drug-discovery:** we employ high-throughput enzymatic assays under anaerobic conditions to target redox processes, including the biosynthesis of iron-sulfur (Fe-S) clusters. This technology has relevance in conditions like Friederichs's ataxia<sup>4</sup> and can advance drug discovery in this field
- **RNA engineering and ribosome manipulation:** our expertise includes the study of RNAs modifications, as well as the ability to manipulate ribosomes to correct a defective gene without modifying the genome. This technology is also valuable for RNA-based gene therapy<sup>5</sup>
- **Mechanotransduction assays for cell adhesion and migration:** we offer *in vitro* assays that reconstitute mechanotransduction of cytoskeletal forces involved in adhesion and migration. These assays use purified proteins and synthetic membranes, presenting exciting opportunities in drug discovery<sup>6</sup>
- **Mitochondrial transformation:** we have developed biolistic transformation techniques for mitochondria in budding yeast and micro-algae<sup>7</sup>. This enables genetic modifications of this organelle without affecting the nuclear DNA
- **Cellular models for vaccine development:** our cellular models are designed to screen drugs that modulate the presentation of antigens by immune cells. This technology is crucial for vaccine development and immunotherapy research<sup>8</sup>
- **C. elegans as a model for the analysis of stress on development and aging:** we utilize the *C. elegans* animal model to study the effects of stress on development and aging, as well as to identify adaptation mechanisms. This model system can provide valuable insights into various biological processes<sup>9</sup>
- **Computational screening and modeling of protein interaction networks:** we have developed computational pipelines to predict how a set of proteins may interact using evolutionary information and deep learning tools<sup>10</sup>. We have acquired particular expertise in dealing with disordered regions in proteins and are able to screen large interactomes using *in silico* two-hybrid technology<sup>11</sup>. We provide expertise on how to engineer the predicted interfaces<sup>12</sup>

## Fields of expertise

- Genome engineering
- Gene therapy
- Cell targeting and anti-tumor activities
- Vaccine development
- Synthetic biology
- Molecular interactions
- Cell stress and proliferation
- Photosynthesis
- Metal homeostasis

## Technical skills

- Manipulation of RNA and ribosome engineering
- Production of novel peptides, proteins and binders
- Characterization and modelling of multimolecular complexes
- Immuno-monitoring of immune responses
- Molecule screening and drug binding analysis
- Biolistic transformation
- Computational biology

## References

1. Campanacci, V. et al. PNAS 116, 9859-9864 (2019)
2. Canu, N. et al. Nucleic Acids Res 48, 11615-11625 (2020)
3. Nikolic, J. et al. Nat Commun 9-1029 (2018)
4. Monfort, B. et al. Front Neurosci 16-838335 (2022)
5. Bidou, L. et al. PNAS 119-2122004119 (2022)
6. Vigouroux, C. et al. Nat Commun 11-3116 (2020)
7. Bonnefoy, N. & Remacle, C. Methods Mol Biol Humana, New York, NY 2615, 345-364 (2023)
8. Sarango, G. et al. EMBO Rep 23-55470 (2022)
9. Chen, Y. et al. J Cell Biol 220- 201909139 (2021)
10. Bret, H. et al. Nat Commun, in press (2024)
11. Leuzzi, G. et al. Cell, in press (2024)
12. Nicolas, Y. et al. bioRxiv, 2023.08.05.552090