08 Accelerator Grants

Expanding the chemical space of bioactive modified nucleotides to endogenous metal ions

Accelerator Grant

- Pedro Beltrao, Dept. of Biology, ETH Zürich, Switzerland
- Clara Correia-Melo, Dept. of Microbiome in Ageing, Fritz Lipmann Institute, Jena, Germany
- Kasper Fugger, Dept. of Cancer Biology, UCL Cancer Institute, UK
- **Christian Hartinger, School of Chemical Sciences, University of Auckland, New Zealand (Aotearoa)**

Nucleotides are the key building blocks of the nucleic acids which contain the genetic code that is fundamental to life. In biology, chemical or enzymatic reactions can structurally modify nucleotides (modNs'). This can result in a large number of modNs that are critical in cellular processes while others can damage biological material. Metal ions play key roles in many biological processes and are central to the function of many enzymes. Metal ions can also react with nucleotides or cause indirect modifications of nucleotides. This project will uncover the formation of modNs after reaction with endogenous metal ions (Me-modNs) in biological systems, a so far unexplored source of nucleotide modification.

This HFSP Accelerator Project will build on research into the diversity of modNs, their modifying-detoxifying enzymes and their evolutionary history, and bioactivity, and will expand the chemical space of modNs to incorporate endogenous metal ions. We will investigate biological samples for the formation of Me-modNs using advanced analytical methodology, will synthesize metal complexes from modNs and investigate them for their biological activity. Beyond endogenous metal ions levels, we will also evaluate the impact of elevated metal ion concentration in the formation of modNs in biological systems.

Overall, this interdisciplinary project will deliver a fundamental understanding of the effects that metal ions have on modNs and the resulting conjugates in biology. For this purpose, we have established an international research team with complementary expertise ranging from cell biology, computation, and analytical chemistry to synthetic inorganic chemistry.

Capturing evolution in action using ancestral genotypes resurrected from sand dune seed banks

Accelerator Grant

- Luke Dunning, School of Biosciences, University of Sheffield, UK
- Valerie Reijers, Dept. of Physical Geography, Utrecht University, Netherlands
- Meagan Wengrove, School of Civil and Construction Engineering, Oregon State University, Corvallis, USA
- **Teresa Konlechner, Dept. of Geography, University of Otago, Dunedin, New Zealand (Aotearoa)**

Measuring rates of evolution is crucial for understanding how species adapt to environmental change. However, a challenge in studying evolution is that we often only see the end result—today's species—without direct evidence of how they got there. This can lead to underestimating the speed of evolution and misjudging future adaptation potential. Resurrection ecology, which involves reviving dormant seeds or propagules from the past, allows us to track these evolutionary changes directly. It is like accessing nature's archive, revealing the true pace of evolution and resilience against environmental change.

In this Accelerator project, we use seed banks and a resurrection approach, alongside expertise in geoscience, genetics and ecology, to measure how fast dune grasses have evolved and what this means for coastal dunes in the future. Ultimately, our goal is to understand how small genetic variations in these grasses lead to physical traits that can drive significant changes in our sandy coasts—specifically, how these traits affect dune shape and stability. Accurate measurements of evolution rates are essential for assessing the grasses' adaptive potential and the ability of sand dunes to respond to ongoing environmental changes.

To do this we will use geoscience methods to map sand layers in dunes where seeds have been buried. These buried seeds are time capsules of genetic material. By growing ancient seeds alongside modern plants, we can directly observe trait changes and calculate the speed of evolution. We will also analyze historical environmental data to track how dunes have shifted over past decades and reconstruct past climates, helping us understand how factors like drought and erosion have shaped dune grass evolution.

This data will be integrated with findings from complementary studies, including DNA sequencing and experiments measuring how plant variation impacts sand trapping ability. We will then develop computer models of virtual dunes to simulate how these genetic and ecological changes affect dune formation over time and their capacity to adapt to future climate challenges.

Understanding how dunes are established and maintained is important, as they protect our coasts from floods and storms. By learning how they work, we can better prepare for a future where climate change and stronger storms may pose significant challenges to our dunes.