Title of Project:	Cotranscriptional features that determine RNA fate
Cell Mechanism Supervisor Name	David Tollervey
Quantitative Supervisor Name	Guido Sanguinetti

Summary of project

Eukaryotic cells generate huge numbers of stable RNAs, mRNAs and ncRNAs, which have substantially different fates, particularly with respect to targeting for rapid degradation by the nuclear RNA degradation system. Features that influence RNA fate include co-transcriptional protein binding, which in turn reflects nascent RNA sequence and folding, the composition of the transcription complex, RNA polymerase modifications and histone modifications. The composition of the transcription complex likely reflects the sequence of both the promoter and the nascent transcript……and there many more potential interactions.

The necessary data will be generated in the Tollervey lab, using high-throughput techniques, where it does not already exist. These will be analysed using machine learning in the Sanguinetti group, with the aim of generating testable hypotheses that will be then be addressed experimentally.

Like many other biological analyses, we will generate very large datasets. However, key features and interactions in these data cannot readily be discerned by traditional reductionist approaches, involving skilled researchers looking through the data. The predictive, integrative and systems approaches that we will adopt, require close collaborations between biologists and informaticians. These will allow the development of integrative models capable of generating biological insights from diverse, high-complexity datasets. Notably, the Tollervey and Sanguinetti groups have an established track record of successful collaboration.

What quantitative skills will the student acquire or develop during their PhD project?

Yeast molecular genetics. Strain contraction using CRISPR techniques.
Generation and analysis of high-throughput sequencing data.
Machine learning approaches to the analysis of multiple datatypes.
All of these skills will be readily applicable to many other projects.