Research

Specialized ribosomes and the control of translation

The ribosome – the cellular machine that translates information in mRNA templates into functional protein – is made up of ribosomal RNAs and about 80 ribosomal proteins. Despite the many components, ribosomes are typically seen as invariant entities. The conventional approach to studying translation has been to treat ribosome recruitment by auxiliary protein factors to mRNA templates as the end-point of translational regulation. However, there has been evidence indicating that the composition of ribosomal proteins in ribosomes can vary and that this in turn leads to distinct phenotypes. This phenomenon has been documented largely in yeast, plants, fruit flies, and zebrafish, but has not been well-studied in mammalian systems, even though many human disorders have been linked with the dysregulation of translation. In particular, there is a class of human genetic disorders known as ribosomopathies, in which mutations occurring in certain genes ultimately lead to impaired ribosome biogenesis and function. The most well-documented ribosomopathy to date is Diamond Blackfan Anaemia – almost half of patients with this disorder have mutations mapping to ribosomal proteins, with as many as 25% mapping to a single ribosomal protein, RPS19, alone.

Ribosome profiling is a recently developed technique used to study translation on a genome-wide level. This high-throughput technique has been demonstrated to provide codon-by-codon resolution of the mRNA locations of translating ribosomes in various organisms, including in mammals. We have previously used ribosome profiling to study microRNA-mediated repression, and are looking to employ this technique in exploring the concept of specialized ribosomes in regulating translation.

Through studying another facet of translational regulatory mechanisms, we hope to gain a deeper understanding of translational control and uncover novel avenues towards therapeutics development.

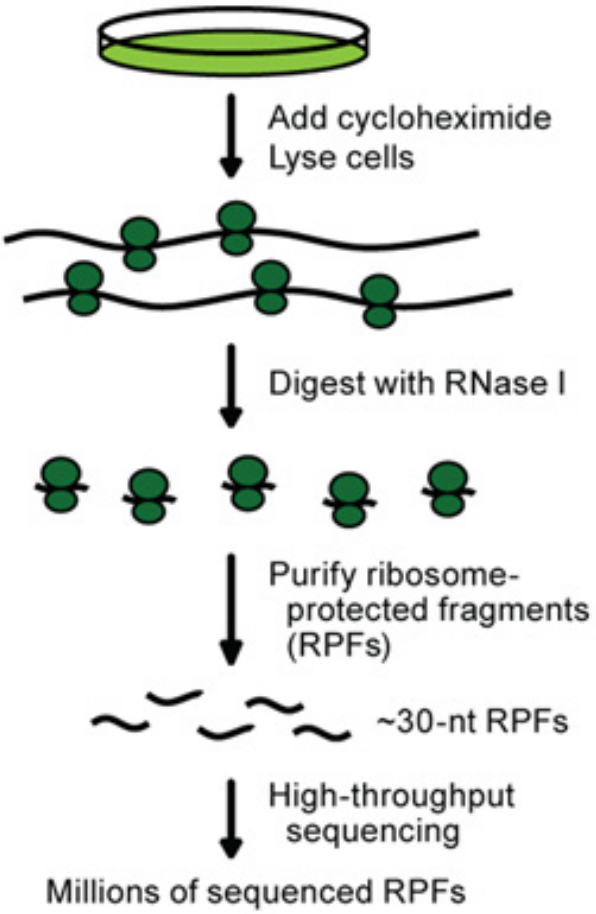

Figure 1. Schematic diagram of ribosome profiling (Guo et al., 2010).

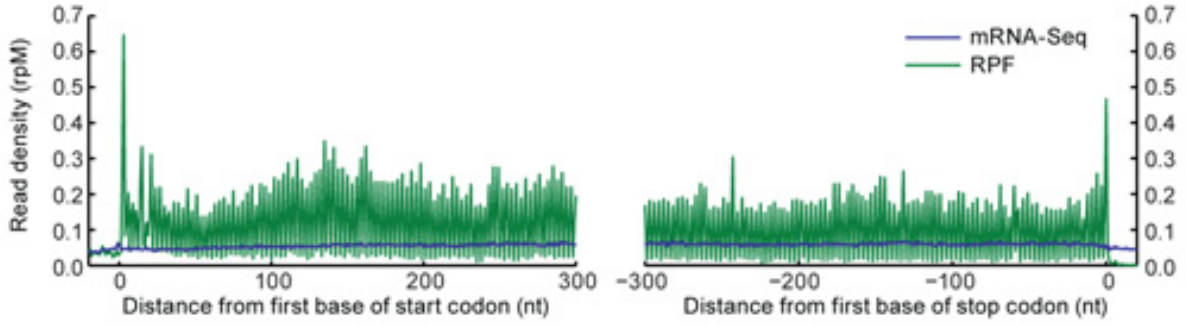

Figure 2. Density of RPFs and mRNA-Seq tags near the ends of open reading frames in HeLa cells. Ribosome profilling is able to capture the characteristic codon-by-codon movement of translating ribosomes (Guo et al., 2010).