Investigation of a novel group of small ribonucleotide reductases

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Class I ribonucleotide reductase (RNR) is an essential enzyme that produces deoxyribonucleotides - DNA building blocks - in an oxygen-dependent manner. The catalytic form of the enzyme is a complex comprised of one large catalytic homodimer, R1, and a small homodimer, R2, which generates an essential radical required for catalysis in R1. Class I RNRs are divided into subclasses, mostly based on the metallocofactor used in radical generation in R2. Both R1 and R2 assume a conserved fold independent of subclass; R1 folds into a unique, 10-stranded α/β barrel, and R2 takes on a ferritin fold. Additional loops and domains like ATP cones and extended C-termini play crucial roles in the regulation of the RNR complex, which are essential components of this enzyme's ability to maintain a balanced deoxyribonucleotide pool.

Recently, a new clade of RNR was discovered, with properties resembling class I RNRs, with sequences for a larger and a smaller subunit. Strikingly, all of these sequences are about one-third shorter than most other RNR sequences found to date. Sequence alignment, alpha fold predictions, and a cryo EM structure show that the overall fold is similar to the described folds of R1 and R2, but that many helices are shorter than usual, that loops are smaller, and the C-termini are much reduced (Burnim et al., 2022).

The presented project aims to characterize this new clade of RNR. How are these small enzymes regulated and do these systems represent a minimal RNR architecture?

References:

Burnim, A. A., Spence, M. A., Xu, D., Jackson, C. J., & Ando, N. (2022). Comprehensive phylogenetic analysis of the ribonucleotide reductase family reveals an ancestral clade. *ELife*, *11*. https://doi.org/10.7554/ELIFE.79790