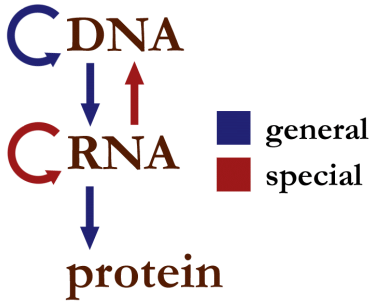
**Reg. No: 2015/19/P/NZ2/03655; Principal Investigator: dr Leszek Piotr Pryszcz**

RNA editing is a process of post-transcriptional alteration of transcripts. As such, RNA editing contradicts central biology dogma of transition of information from gene (DNA), through transcript (RNA), to protein, as due to RNA editing the primary sequence of particular transcripts can be altered, resulting in altered protein sequences that does not necessarily correspond to the sequence



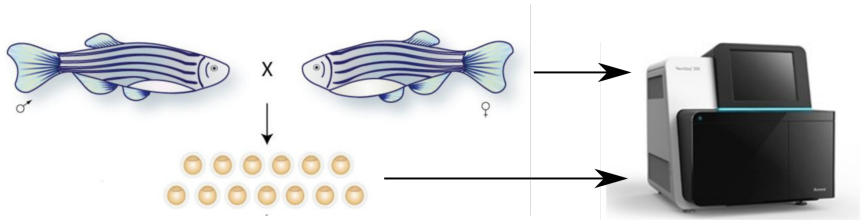

of the gene.

RNA editing was described for the first time in the 1980s, so it isn't a new discovery. Since then, RNA editing was characterised in numerous organisms and it has been reported to function in an array of biological processes. RNA editing affects physiology and behaviour of animals from insect to human, by altering both, the sequence and structure of nervous system components. The most interesting roles of RNA editing described so far are: determination of castes in ants, adaptation to cold in octopuses. Most of all, RNA editing is crucial for correct development of the brain and nervous system of animals.

In addition, RNA editing was proposed to protect human (and other primates) genome against the expansions of Alu elements. Alu elements are repetitive sequences that are very abundant in our genome. What is more, Alu elements are believed to destabilise the genome by copying themselves across the chromosomes through the process of retrotransposition (transposition involving RNA). ADAR, one of the enzymes responsible for RNA editing, was found to bind Alu transcripts, edit their sequence and therefore block subsequent transposition to new genomic locations.

Besides extensive research and multiple proposed functions in various organisms, there is still no consensus for the biological purpose of RNA editing. We would like to study the role of RNA editing in developing embryo. Obviously, we cannot conduct this study in human, therefore we will use zebrafish (Danio rerio), as it is easy to maintain in the lab and gives access to very early developmental stages, while being relatively close to human (we share approximately 70% of genes with zebrafish).

We will characterise RNA editing in zebrafish, by sequencing parental genomes and the transcriptomes of developing embryos at several stages of development. As RNA editing is expected to create differences between transcripts and genome sequence, subsequent comparison of transcripts with the genome sequence it is encoded from will allow genome-wide detection of RNA editing. This will allow us not only to create the most comprehensive RNA editing catalogue of developing embryo, but also to identify the changes in RNA editing throughout embryo development.




Furthermore, we will remove RNA editing system from zebrafish by knocking out adar, the enzyme responsible for RNA editing. This will allow us to confirm the necessity of RNA editing in early embronic development and help to confirm its target RNAs identified by sequencing. In addition, we will be able to characterise the effects of missing RNA editing, and therefore hypothesize about its role in developing embryos. Moreover, by comparing the changes in gene expression and regulation in control and mutant, we will be able to identify molecular targets of RNA editing. This will serve as additional line of evidence for the role of RNA editing in embryonic development.

Finally, we plan to conduct a series of molecular and biochemical experiments to characterise the RNA editing roles and to confirm our finding about its function in development.