ABSTRACT:

Mast cells are tissue resident members of the immune system. They have a wide range of functions and receptors including the FcεRI receptor, which gets activated by binding to IgE bound to an antigen. When the cells are activated in this manner, a process termed the LysRS-Ap4A-MITF signalling pathway occurs, resulting in the translocation of the Lys tRNA synthetase into the nucleus and an activation of its moonlighting activity – the production of diadenosine tetraphosphate (Ap_4A). Ap_4A is a dinucleoside polyphosphate, a type of ubiquitous molecule present in all domains of life. They are made up of two nucleosides joined together by a 5' to 5' phosphodiester bridge of variable lengths. Recently, these molecules have been shown to serve as non-canonical initiating nucleotides during bacterial transcription, where they function as 5' RNA caps, similar to the well-known 7-methylguanosine eukaryotic mRNA cap. In this thesis, I present proof of existence of Ap_4A capped RNA in mast cells, a previously unknown 5' RNA structure in eukaryotic cells, and I attempt to pinpoint its role in the activation of these cells and in the wider context of mast cell mediated immune response.

Keywords: mast cells, RNA caps, Dinucleoside polyphosphates, Ap_4A, RNA modification, IgE, FcεRI receptor, Lysine tRNA synthetase