PhD DEFENCE Friday, May 5th, 2017
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Title: USING PATHOGEN INACTIVATION TREATMENT TO STUDY THE STABILITY OF PLATELET MESSENGER RNA
Time and location: 9:00am PDT; Room 202, Anthropology and Sociology Building, UBC Point Grey Campus
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ABSTRACT

Pathogen inactivation (PI) techniques are designed to increase the safety of blood products by damaging RNA and DNA of pathogens. Even though platelets are anucleate, they synthesize proteins using RNA and the ribosomal machinery derived from megakaryocytes. The role of protein synthesis in platelets, however, is still poorly understood. PI-treated platelets show signs of accelerated storage lesion, but the effect of PI on platelet mRNA and subsequent protein synthesis remains unclear. In this dissertation we investigated to what extent platelet mRNA is affected by PI using Mirasol as a representative PI.

In this dissertation we demonstrated that the Mirasol treatment affected platelet mRNA negatively in a target specific manner, but prolonged the mRNA half-life. The long mRNA half-life suggested the presence of a mechanism, protecting platelet mRNA from degradation. We investigated the role of p38 MAP kinase (p38MK) as a potential regulator of platelet mRNA and whether stress granule (SG) formation could be involved in protecting platelet mRNA.

The kinase p38MK is a key regulator of a wide range of platelet function. In nucleated cells, UV-induced stress activates p38MK and ultimately leads to increased mRNA stability through the regulation of RNA binding proteins. UV illumination is a key feature of all PI techniques, and p38MK is activated in Mirasol-treated platelets. In this dissertation we demonstrated that inhibition of p38MK in Mirasol-treated platelets increased the mRNA half-life, but not through the RNA binding proteins human antigen R or tristetraprolin.

SG formation is a protective response in nucleated cells to temporarily store mRNA. SG consists of mRNAs and specific SG proteins. This dissertation contained a description of the preliminary experiments performed to test the effect of a known SG inducer (arsenite) and inhibitor (nocodazole) in platelets, especially in the context of the Mirasol treatment. Nocodazole did not impact the platelet mRNA levels, but affected the mean platelet volume and count in Mirasol-treated platelets. Arsenite exposure did not affect platelet total RNA or GAPDH mRNA, but showed a reduction in extent of shape change. Our experiments showed that platelets possessed the potential to form stress granules, but a definitive mechanism was not demonstrated.