

PhD DEFENCE Monday, November 27th, 2017

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Title: RED BLOOD CELL HEMOLYSIS: PROTEIN BIOMARKER DISCOVERY FOR PRODUCT QUALITY ASSESSMENT

Time and location: 12:00pm PST; Room 418, MacLeod Building, 2356 Main Mall, UBC Point Grey Campus

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ABSTRACT

Red blood cell (RBC) transfusion is a cornerstone therapeutic intervention in contemporary medicine. Stored RBCs undergo multiple biochemical and biophysical changes, collectively referred to as the RBC storage lesions. One of the most prominent alterations is hemolysis, the rupturing of RBC and the subsequent release of hemoglobin-rich cytosolic content. Hemolysis may compromise the red cell concentrate (RCC) therapeutic efficacy with a decrease in viable and functional cells and an increase in bioactive molecules that may disrupt vascular and immune homeostasis. Thus, hemolysis is used as a key surrogate indicator of RCC storage quality; however, this parameter is evaluated at expiry and all RCCs are transfused without knowing their hemolysis levels. With aims to optimize product quality for recipients and to improve donor and inventory management efficiency, the identification of predictive markers for storage hemolysis warrants further investigation.

While the precise molecular mechanism(s) of storage-related hemolysis remain elusive, a few factors such as donor characteristics and manufacturing processes are known to influence its development. From a unique donor population composed of repeat donors exhibiting high hemolysis, membrane-associated proteins involved in antioxidant pathways - peroxiredoxin-2, catalase, and 20s proteasome - were identified as potential quality markers using isobaric tag for relative and absolute quantitation. Additionally, in a novel comparative study between RCC subjected to gamma-irradiation and pathogen inactivation (PI), the level of these candidate protein markers displayed robust negative linear relationship with storage hemolysis. These candidate protein markers hint at the role of oxidative damage in product quality deterioration and hemolysis development. While deoxygenation treatment successfully rescued elevated hemolysis in PI-treated RCCs, the application of these protein markers did not yield similar relationship to hemolysis development. This observation suggests that PI-induced damage is heavily reliant on the presence of oxygen and that the identified protein quality markers may not be specific to oxidative damage alone.

Taken together, the findings presented here propose three potential candidate protein markers for product quality and further support that cumulative oxidative damage contributes to storage hemolysis development. However, the results suggest that there may be additional underlying metabolic and/or molecular mechanisms that are important for hemolysis development.