SP10* High sensitivity blood analyte assays: Marcos Dantus, Michigan State University
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Associated With: TRD3

Significance: As recent events have demonstrated, the supply of donated blood products is crucial for patients following trauma. The shelf life of blood products in storage has largely been determined by looking at the average lifetime of these supplies, rather than individual blood samples themselves. However, samples can expire early, such that patients receive substandard blood supplies that affect patient mortality (2-7), or survive longer than the average, in which case lifesaving supplies are thrown away. For example, red blood cells (RBCs) are stored for a total shelf life of 42 days, but some samples outlive this time period. In the case of platelets, the storage time is much shorter – 5 days at room temperature with constant agitation to prevent loss of platelet function - leading to 1.6 million units discarded annually. A toolkit that allows for the inspection of blood components, either during storage or at the time of transfusion, would enable the safe supply to patients and also extend the storage of blood products to stretch already limited supplies.

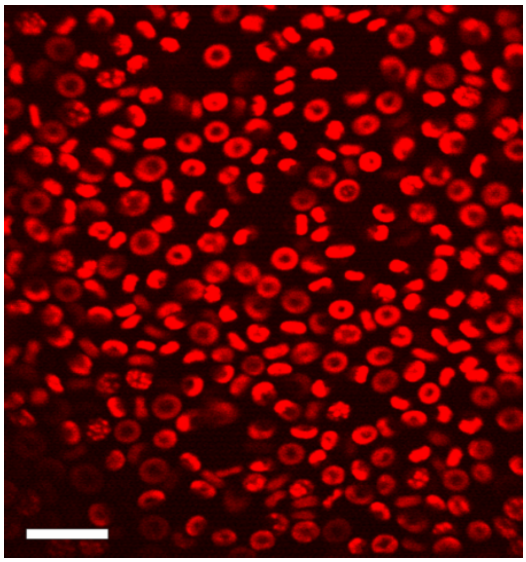

Figure 1 – TPEF image of unstained human RBCs on a glass coverslip. Scale bar: 20 μm.(1)

Dr. Marcos Dantus, a Professor at Michigan State University and expert in nonlinear physics and microscopy, has been investigating the endogenous emission from RBCs to create imaging tools for the inspection of blood samples. In a recent collaboration between the Dantus and Evans laboratories, the Dantus group made use of several nonlinear imaging techniques including two-photon excitation fluorescence (TPEF) and third harmonic generation (THG) microscopies, to investigate RBCs in storage. The Evans laboratory, in providing data from our coherent Raman (SRS) and transient absorption (TA) microscopy system, aided the Dantus group in developing a preliminary toolkit that can visualize RBC morphology through the blood storage bag without compromising sterility (1).

Approach: The Dantus group aims to develop imaging systems that can be translated for the testing of blood products, based on compact sub-40fs femtosecond fiber lasers (8, 9). While two-photon and third harmonic microscopy were found promising to visualize cells with endogenous contrast, coherent Raman and transient absorption imaging may also be helpful in complementary, quantitative imaging of blood components. In order to determine the optimal set of imaging parameters, the Dantus lab will work with the LBRC to use SRS and TA imaging of RBCs – specifically the shape and deformability of the cells. These functional parameters are important for proper RBC function; as the cells age, they can lose the flexibility that allows them to flow through narrow vessels and capillaries (10, 11). Measurements made at the LBRC will be matched with experiments in the Dantus lab to determine an optimal set of imaging and microscopy parameters for in-bag analysis. Testing will be ultimately performed on human blood bags to track RBC decline and map blood product lifetime. If successful, this toolkit may be extended for the imaging of platelets.

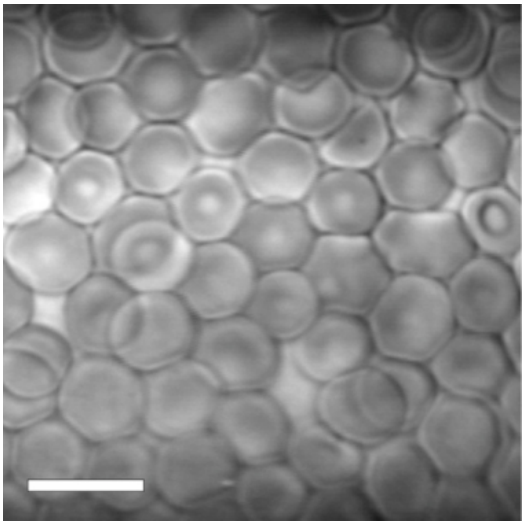

Figure 2 – THG image of human RBCs acquired through the storage bag. Scale bar: 10 μm.(1)

Center Offering: The LBRC offers coherent Raman imaging tools via the Evans laboratory at the Wellman Center for Photomedicine that will provide the Dantus team with imaging resources for their study. The laboratory offers a multimodal automated coherent Raman microscope that has additional confocal, multiphoton, FLIM, and TA microscopy components needed for the Dantus project. In addition to the imaging platform, the LBRC provides experience in the design and implementation of coherent Raman and other nonlinear microscopies, which will be helpful to the Dantus team as they translate their imaging system forward. Furthermore, the Dantus team will have access to image analysis expertise within the LBRC, including individuals with prior experience in the analysis of RBC membrane dynamics. These experiences will be important in providing the Dantus laboratory with the tools needed for successful clinical translation.

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