



SELECTED PUBLICATIONS

Metal-activated C-peptide Facilitates Glucose Clearance and the Release of a Nitric Oxide Stimulus via the GLUT1 Transporter, J. Meyer, J. Froelich, W. Karunaratne, G. Reid, and D.M. Spence, *Diabetologia* **2008**, 51, 175-182.

Measuring the Simultaneous Effects of Hypoxia and Deformation on ATP Release from Erythrocytes, A. Faris and D.M. Spence, *Analyst* **2008**, 133, 678-683.

Red Blood Cell Stimulation of Platelet Nitric Oxide Production Indicated by Quantitative Monitoring of the Communication between Cells in the Bloodstream, J. S. Carroll, C.J. Ku, W. Karunaratne, and D. M. Spence, *Anal. Chem.* **2007**, 79, 5133-5138 (accelerated article).

Addressing a Vascular Endothelium Array with Blood Components using Underlying Microfluidic Channels, L.Genes, N.V. Tolan, M. Hulvey, R.S. Martin, and D.M. Spence, *Lab on a Chip* **2007**, 7, 1256-1259.

An Altered Oxidant Defense System in Red Blood Cells Affects their Ability to Release Nitric Oxide-Stimulating ATP, J. Carroll, W. Subasinghe, M. Raththagala, S. Baguzis, T.D. Oblak, P.D. Root, and D.M. Spence, *Molecular Biosystems* **2006**, 2, 305-311 (cover article).

ASSOCIATE PROFESSOR

(b. 1970)

B.S., 1992,

Grand Valley State University

Ph.D., 1997,

Michigan State University

Assistant Professor,

1997-2002,

St. Louis University

Associate Professor,

2003-2004,

St. Louis University

Associate Professor,

2004-2007,

Wayne State University

517-355-9715

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A growing body of literature exists suggesting novel roles for red blood cells (RBC) *in vivo*. Our group was the first to report that the RBCs obtained from people with type 2 (or adult-onset) diabetes released less ATP upon stimulation in comparison to RBCs obtained from non-diabetic subjects. The importance of this finding is due to the role of ATP in controlling blood flow, endothelial cell function, and platelet function.

Recently, our group has also made another important discovery that we hope will change the way in which insulin is administered. Specifically, we have determined that C-peptide, an acidic 31 amino acid peptide that is co-released with insulin in the beta cells of the pancreas, can be activated using a metal (such as zinc). In the absence of the metal, there is no activity; however, in the presence of the metal, the C-peptide is able to stimulate glucose intake by the RBCs. Moreover, the end result of this glucose uptake is an increase of ATP release from the RBC. This finding will be important for future experiments involving C-peptide, especially because most scientists have believed for over 40 years that C-peptide is a non-bioactive substance.

Another theme that seems to be taking hold in our group and will be further investigated in the near future is a concept which we have initially labeled as "metabolic shifting analysis". This concept is not necessarily new; in fact, it is known that many metabolic pathways in cells have inhibitory feed-

back mechanisms. However, our group will be attempting to demonstrate that some pathways only begin when another pathway has reached its maximum operating velocity. An example of this is two pathways in RBCs known as the pentose phosphate pathway and the aldose reductase pathway.

Our group believes that the aldose reductase pathway becomes more active when the pentose phosphate pathway reaches a maximum velocity. The implications of these competing pathways may play major roles in how RBCs utilize glucose.

Overall, the primary goal of our research is to gain a molecular level understanding of the role of the RBC in various diseases. The objectives that must be accomplished in order to reach that goal are centered around designing methods that enable measurements

to be performed on samples (e.g., red blood cells, endothelial cells, and platelets) in an environment that closely mimics true physiological conditions. For example, the figure shown is an image taken by our group of a microfluidic device used to determine NADPH levels in diabetic RBCs. Collectively, creating such biomimetic systems requires a working knowledge of analytical chemistry, biomaterials, physiology, molecular and cell biology, and microfluidics. Our group applies these skills to the development of unique schemes that can help answer important biomedical questions.

50 μM NADPH

25 μM NADPH

12.5 μM NADPH

5 μM NADPH

2.5 μM NADPH

7% Lysed RBCs

