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## Inhibitor of differentiation 3 blocks oxidized phospholipid induction of monocyte chemotactic protein-1 in vascular smooth muscle cells

Coleen McNamara, Jack Hensien, Aidan Toms and James Garmey University of Virginia Health System, USA

**Background:** Atherosclerosis, the most common cause of death worldwide, is a chronic inflammatory disease initiated by accumulation of oxidized phospholipids (oxPL) in the artery wall. OxPL in arteries induce vascular smooth muscle cells (VSMCs) to produce chemokines such as monocyte chemotactic protein-1 (MCP-1), which attracts monocytes to the artery. Inhibitor of differentiation 3 (Id3) is a transcription factor that has been shown to limit artery plaque buildup in mice. Humans with a specific single nucleotide polymorphism (SNP) in Id3 have greater artery plaque buildup, underscoring the relevance of identifying pathways whereby Id3 may regulate artery plaque buildup.

Hypothesis: OxPL induces expression of more chemokines, such as MCP-1, in VSMCs lacking Id3 compared to control.

**Methods and Results:** Cultured VSMCs with the Id3 gene deleted and control VSMCs were stimulated with oxPL, harvested 24 hours later and mRNA was isolated. The mRNA was reverse transcribed and then specific mRNA was quantitated using polymerase chain reaction (PCR). Loss of Id3 increased MCP-1 expression in VSMCs treated with oxPL. OxPL-induced expression of another chemokine unrelated to macrophage chemotaxis, CCL11, was not Id3-dependent.

**Conclusions:** Id3 may be an important factor that limits MCP-1 expression and monocyte infiltration in the artery wall and humans with the Id3 SNP may have increased plaque due to loss of Id3 inhibition of MCP-1 expression in VSMCs. The Id3 SNP may be able to identify humans that could benefit from local delivery of inhibitors of MCP-1.

## Biography

Inhibitor of Differentiation 3 Blocks Oxidized Phospolipid Induction of Monocyte Chemotactic Protein-1 in Vascular Smooth Muscle Cells. Jack Hensien, Aidan Toms, James Garmey and Coleen McNamara Cardiovascular Research Center, University of Virginia Health System.

Jack Hensien and Aidan Toms are students in the Math, Engineering and Science Academy at Albemarle High School. They performed this work as part of a research assignment in the laboratory of Dr. Coleen McNamara. Mr. Garmey is the laboratory manager in the McNamara lab. Dr. McNamara is the Edward W. and Betty Knight Scripps Professor of Medicine/Cardiovascular Division at the University of Virginia. Her laboratory studies the role of inhibitor of differentiation 3 and vascular and immune cells in the development of atherosclerosis using murine models and through translational human studies.

CAM8C@hscmail.mcc.virginia.edu