Plvap/PV1 critical to formation of the diaphragms in endothelial cells

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Dartmouth scientists have demonstrated the importance of the gene Plvap and the structures it forms in mammalian physiology in a study published in December by the journal *Developmental Cell*.

"The knowledge generated and the animal models created will allow a better understanding of the role of the gene in diseases and will help validate its usefulness as a therapeutic or diagnostic target," said lead author Radu V. Stan, MD, associate professor, Geisel School of Medicine at Dartmouth, and member of the Dartmouth-Hitchcock Norris Cotton Cancer Center (NCCC).

The study demonstrates that plasmalemma vesicle associated protein (PV1), a vertebrate gene specifically expressed in the vascular endothelial cells, is critical for the formation of the diaphragms of endothelial caveolae, fenestrae and transendothelial channels. Although discovered in the 1960s by electron microscopy, the function of the diaphragms was previously unknown. Using mice with loss and gain of PV1 function Dartmouth scientists demonstrated that the diaphragms of fenestrae are critical for maintenance of basal permeability, the homeostasis of blood plasma in terms of protein and lipid blood composition, and ultimately survival.

PV1 has newly discovered roles in cancer and in various infectious and inflammatory diseases. "The knowledge generated and the animal models created will allow a better understanding of the role of the gene in these diseases and to validate its usefulness as a therapeutic or

diagnostic target," said Stan.

In the absence of such diaphragms, plasma protein extravasation produces a noninflammatory protein-losing enteropathy resulting in protein calorie malnutrition and ultimately death.

"Our results and the mouse models we have created provide the foundations for evaluating numerous aspects of basal permeability in fenestrated vascular beds," said Stan.

Provided by Dartmouth-Hitchcock Medical Center