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**Structural Study of the Inhibition of Endothelial Nitric Oxide Synthase by a Caveolin-1 Scaffolding Domain Peptide**

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Nitric oxide (NO) derived from endothelial nitric oxide synthase (eNOS) is a ubiquitous signaling molecule that is necessary for vascular remodeling, angiogenesis, wound healing, and maintenance of systemic blood pressure. Caveolin-1 is a member of the protein family of caveolins, integral membrane cholesterol-binding proteins, which constitute the main building block of caveolae. Furthermore caveolins have been shown to be involved in regulation of a variety of signal transduction pathways. Being a peripheral membrane protein, eNOS is targeted in caveolae where it can physically interact with caveolin-1 by binding to its putative scaffolding domain located between amino-acids 82 to 101. A peptide corresponding to this particular caveolin-1 region has been demonstrated *in vivo* to have the ability to selectively block eNOS function leading to the inhibition of acetylcholine-induced vasodilation and NO production in endothelial cells. Furthermore, when administered systematically in mice this peptide can also suppress acute inflammation and vascular leakage to an extent comparable with glucocorticoids. The elucidation of the molecular basis of the mechanism of inhibition of eNOS by this peptide is a cornerstone for the development of new therapeutic approaches to inflammation. We are employing x-ray crystallographical methods toward this end.