

**P025** The role of non-conserved active site residues in substrate specificity of AOC3

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Leukocyte trafficking from blood vessels happens via an extravasation cascade. Vascular adhesion protein-1 (VAP-1, AOC3) is involved in the rolling and transmigration steps of the cascade by an enzymatic-activity dependent manner: The semicarbazide-sensitive amine-oxidase (SSAO) activity of AOC3 is required for its adhesive functions. Among amine oxidases AOC3 is unique with its adhesion property. Other amine oxidases do not function as adhesion proteins even though solved atomic structures are similar. Also the substrate preference towards tested primary/ aromatic amines differs among species/source. The solved structures reveal differences in the substrate cavity, which plausible cause the variation in substrate specificity: several non-conserved amino acid residues are lining the cavity leading to the active site. According to homology modeling of another human SSAO, AOC2, these residues differ also between AOC2 and AOC3. In this study three of these residues in AOC3 were mutated to the corresponding ones in AOC2. The effect of the mutations M211V, Y394N and L469G on the enzymatic activity was assayed using different known amine substrates. The results show that the mutations affect on the substrate specificity. The effect of the mutations on the leukocyte adhesion will be tested in the future. The information about the roles of the active site residues in primary amine binding will help us when identifying the real, physiological leukocyte counterpart of VAP-1, which is unidentified.