Vasoactive Peptides Processing in Murine MAB Perfusate

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The rat MAB perfusate is a rich source of vasopeptidases, among which elastase-2 has been recognized as the major angiotensin II-forming enzyme and carboxypeptidase B the only conspicuous bradykinin-cleaving enzyme. Besides, a perfused rat MAB secretes a considerable amount of thus far uncharacterized CPA-like enzymes which endows the corresponding perfusate with efficient angiotensin-processing pathways. To further understand the physiological importance of these enzymes in the local peptide metabolism of the mesentery we compared both the proteolytic compositions of rat and mouse MAB perfusates, and the expression of mRNAs for various proteases in the mesentery of these murine species. The patterns of the rat MAB perfusate-catalyzed cleavage of AI, AII and BK were similar to those analogously generated by the mouse perfusate, as determined by HPLC analyses. It was also observed that both MABs released into the corresponding perfusate a comparable amount, on a per min basis, of the various peptidases. The protease inhibitors SBTI, PCI, o-phenanthroline and MGTA interfered equally with the proteolytic actions of rat and mouse perfusates. The elastase-2, CPB and CPAs 1-6 mRNA expressions in both rat and mouse mesenteries were evaluated, indicating that only elastase-2, CPB, CPA1, CPA2 and CPA3 mRNAs were present in these tissues. Our results suggest that both rat and mouse MAB perfusates contain the same proteolytic array capable of forming des-Arg9 BK from BK, converting Ang I to Ang II, and generating Ang 1-9 and Ang 1-7 from Ang I and Ang II, respectively. The expression of CPA3 mRNA in murine mesentery suggests that CPA3 might be the protease responsible for Ang 1-7 formation in the MAB perfusate.