CHARACTERIZATION OF THE RECEPTOR MEDIATING THE PROSTAGLANDIN-INDUCED DILATION OF AORTIC VASCULAR SMOOTH MUSCLE IN THE DOGFISH SHARK, *SQUALUS ACANTHIAS*.

David H. Evans[1] and Joanna Nowacki[2]
[1]Department of Zoology, University of Florida, Gainesville, FL 32611
[2]Department of Zoology, University of Wisconsin, Madison, WI 53706

Our previous studies have determined that the endothelium-derived relaxing factor in the ventral aorta of the shark is a prostaglandin (PG) rather than nitric oxide (Evans, D.H. and Gunderson, M.P., Am. J. Physiol. 274: R1050-R1057, 1998). We found that either prostacyclin (PGI_2) or an E-type prostaglandin (PGE_1) produced a concentration-dependent response and that the secretion of both PGs from incubated aortic rings were increased when the calcium ionophore (A23187) was added. However the specific PG receptor mediating the response was unclear, especially since both PGI_2 and PGE_1 can interact with either I- or E-type PG receptors (termed IP and EP; Coleman, R.A. et al., In: *Comprehensive Medicinal Chemistry*, Hansch, C. et al, Pergamon Press, Oxford, 1990). Four EP receptors have been characterized and cloned (designated EP_{1-4}): EP_2 and EP_4 are thought to mediate vascular dilation, while EP_1 and EP_3 are thought to mediate constriction (e.g., Coleman, R.A. et al., Pharmacol. Revs. 46: 205-229, 1994). Fortunately, relatively specific agonists are available which allow the differentiation of these receptor sub-types.

Isolated rings of the ventral aorta from *S. acanthias* were prepared as described previously (Evans and Gunderson, *Ibid*). To characterize the subtype of PGE receptor in the aorta, we added increasing concentrations of either Butaprost (EP_2-specific) or Sulprostone (EP_1- and EP_3-specific; both from Cayman Chemicals), after an initial contraction of the paired rings with 0.1 uM endothelin. Table 1 presents the change in tension (mg) produced by the added Butaprost or Sulprostone (N = 6).

Treatment	**1 nM**	**3 nM**	**10 nM**	**30 nM**	**100 nM**	**300 nM**	**1000 nM**
Butaprost	-6.61±11	-52.3±17.4	-121±38.5	-196±52.8	-374±87.7	-615±134	-769±229
Sulprost.	11.3±7.49	5.96±20.6	10.9±26.9	34.2±36.1	68.3±66.1	210±102	492±63.3

Butaprost dilated the rings in a concentration-dependent manner. The dilation was statistically significant at and above 3 nM. Sulprostone produced an apparent, concentration-dependent constriction, which only reached statistical significance at 1 μM. Our data support the conclusion that the dilation produced by PGs in the shark ventral aorta is mediated by an EP_2-type receptor and suggest that a constrictory, EP_1- or EP_3-type receptor is also expressed. The relative roles of these prostaglandin receptors in controlling vascular diameter in elasmobranchs are unknown at present. (Supported by NSF IBN-9604824 to DHE)