THE TELEOST HEART:

A CONCEPTUAL TOOL FOR STUDIES

OF INTRACARDIAC SIGNALLING

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EXTENDED ABSTRACT ONLY- DO NOT CITE

Recent evidence from both mammalian and non-mammalian vertebrates supports a role for paracrine modulation of myocardial function by the endocardial endothelium (EE) cells. Like the secretory function of the vascular endothelium, this role involves the release of cardioactive factors such as nitric oxide (NO), endothelin-1, atrial natriuretic peptides, prostanoids and a number of other substances that have been well characterised in bioassay studies. Endothelial cells also possess enzymatic activities, in particular ACE/kininase activity, which can alter local levels of angiotensin II and bradykinin.

Using isolated working heart preparations of teleosts (Imbrogno et al., 2001; Gattuso et al., 2002) and amphibians (Sys et al., 1997) previously set up in our lab, we have explored the role of the EE as a source of cardioactive substances and as a sensor of luminal blood flow-related mechanical and chemical stimuli. To analyse the specific autocrine role of the EE without the confounding effects of the vascular endothelium, we used as a natural model juvenile eel (fresh water *Anguilla anguilla*) hearts in which the compact ventricular layer and the coronary circulation are poorly developed.

We found that under basal conditions the EE produces NO in amounts sufficient to exert a negative inotropism on the myocardium via a cGMP-dependent mechanism. The NO signal is abrogated by the functional damage of the EE, indicating that EE transduces mechanical stimulation into NO release. The EE mediates via a NO-cGMP pathway the positive inotropism elicited by luminal

cholinergic stimuli, hence partecipating in the ventricular fine-tuning of the molecular signalling cascade downstream from the stimulation of the cardiac muscarinic receptors (Imbrogno et al., 2001). Moreover, the functional integrity of the EE is a prerequisite for mediating intracavitary Angiotensin II-mediated inotropic signals, since these are abolished by functional damage of the EE by Triton X-100 (Imbrogno et al., 2002, present Symposium).

Of particular interest is the NO-mediated modulation of the Frank-Starling relationship, which emphasises the autocrine-paracrine role of the EE in the intrinsic control of the teleost heart (Imbrogno et al., 2001).

Taken together, these data provide clear evidences for a major cardiac role of NO in fish. After about forty years since the intriguing synopsis of Randall (1968), the emerging importance of this autocrine-paracrine modulation adds further reason for "consolation to fish" in comparison with the "Shepherd's dogs".

References

Gattuso, A., R. Mazza, S. Imbrogno, A. Sverdrup, B. Tota and A. Nylund. 2002. Cardiac performance in *Salmo salar* with infectious salmon anaemia (ISA): putative role of nitric oxide. Dis Aquat Org. In Press

Imbrogno, S., L. De Iuri, R. Mazza and B. Tota. 2001. Nitric oxide modulates cardiac performance in the heart of *Anguilla anguilla*. J. Exp. Biol. 204: 1719-1727

Imbrogno, S., D. Scorpiniti, M.C. Cerra and B. Tota. 2002. The inotropic influence of Angiotensin II on the working heart of the eel (*Anguilla anguilla*): paracrine aspects and subcellular mechanisms. Present Symposium

Randall, D.J. 1968. Functional morphology of the heart in fishes. Am. Zoologist. 8: 179-189

Sys, S.U., D. Pellegrino, R. Mazza, A. Gattuso, L.J. Andries and B. Tota. 1997. Endocardial endothelium in the avascular heart of the frog: morphology and role of nitric oxide. J. Exp. Biol. 200: 3109-3118