Cardiac primitive cells in the adult human heart are influenced by Angiotensin II in chronic heart failure

Daria Nurzynska1, Franca Di Meglio1, Clotilde Castaldo1, Rita Miraglia1, Veronica Romano1, Anna Maria Sacco1, Valeria Barbato1, Giuseppina Granato1, Immacolata Belviso1, Ciro Bancone2, Alessandro Della Corte2, Stefania Montagnani1

1 Department of Public Health, University of Naples "Federico II, 80131 Naples, Italy
2 Department of Cardiothoracic Sciences, Second University of Naples, 80131 Naples, Italy

Angiotensin II (AngII) levels are often increased in patients with cardiovascular disease and different AngII receptor (ATR) blockers are commonly used in heart failure therapy. An increase in number of cardiac primitive cells (CPCs) has been found in adult human pathological heart and these cells express AT1 and AT2 receptors (ATR). Hence, it is conceivable that AngII and ATR blockers influence CPC properties. In this study we investigated the effects of AngII and AT1R, AT2R blocking on human CPCs in vitro.

CPCs were isolated from adult human hearts with ischemic cardiomyopathy (n=11) by tissue digestion and adherent CD117(+) cells immunomagnetic separation. Cells were cultured in the presence of AngII 0,1 and 1µM for 24 hr with and without pretreatment with 1µM valsartan - AT1R blocker (AT1RB), 1µM PD 123319 - AT2R blocker (AT2RB), 10µM telmisartan - AT1RB with PPAR activity, 1µM GW9662 - PPARγ blocker (PPARβ). The expression of PPARγ was evaluated by electrophoresis and immunoblotting, while the proliferation of cells was evaluated by MTT assay.

Administration of AngII stimulated proliferation of CPCs. The expression of PPARγ increased 8,5 and 11,8-fold (p<0,05, n=3) in the presence of 0,1 and 1µM AngII, respectively. In the presence of AT1RB, proliferation of cells did not change significantly but it increased 1,5 and 2,1-fold (p<0,05, n=3) after addition of 0,1 and 1µM AngII, respectively, suggesting that this effect was modulated by stimulation of AT2R.

The results indicate that AT1RB increases CPC proliferation mostly at higher AngII concentrations, while AT2RB has similar effect in the presence of low AngII levels. Hence, complex interactions between AngII and both AT1 and AT2 receptors take place in heart failure patients and influence the survival of CPCs in concentration dependant manner.

Keywords
Cardiac primitive cells, angiotensin II, angiotensin II receptors, cell proliferation.