Supplementary data

Materials and Methods

Data mining

ProteinQuest™ literature mining tool (BioDigitalValley S.r.l., Pont-Saint-Martin, Aosta, Italy) was used to detect correlations and interactions in the β-adrenergic receptor downstream signaling pathways. In particular, the query ["Adrenoceptor beta proteins" AND Myocardium AND ("Heart Failure" Or "Myocardial Ischemia")] was investigated. The analysis of literature obtained by the ProteinQuest™ mining tool detected 344 papers, from which 114 network nodes (proteins) and 499 edges (interactions) were retrieved. Reactome FI app [1] for Cytoscape [2] version 3.2.0 (http://www.cytoscape.org) was employed to analyse pathways and networks (Fig. S1). Among these, Caveolin-3 (CAV3) and PI3K, as well as Src kinase (retrievable as linked to PI3K in further analysis refinements), were assessed for their involvement in cell survival. The role of TIMP1 and MMP2 were investigated to address the fibrosis onset. β-myosin heavy chain (MYH7, β-MHC) was employed as marker of hypertrophy, while TGF-β1 was recruited as marker of both fibrosis and hypertrophy.

Supplementary references

1.   G. Wu, E. Dawson, A. Duong, R. Haw and L. Stein, *F1000Research*, 2014, **3**, 146.

2.   P. Shannon, A. Markiel, O. Ozier, N. S. Baliga, J. T. Wang, D. Ramage, N. Amin, B. Schwikowski and T. Ideker, *Genome research*, 2003, **13**, 2498-2504.

Supplementary figure legends

Figure S1 Data mining. Reactome FI representation of the analysis performed by Protein Quest™. β_1AR and β_2AR where circled in red while the main actors and object of our investigation were highlighted in yellow. Coloured areas represent cell survival (green), fibrosis (blue), hypertrophy (red), or their ovelapping.