Gene profiling in ductus arteriosus and aorta: a question of consistency

Flavio Coceani, Francesca Scebba & Debora Angeloni

The Journal of Physiological Sciences

ISSN 1880-6546
Volume 61
Number 5

J Physiol Sci (2011) 61:443-444
DOI 10.1007/s12576-011-0161-z

Springer

J Physiol Sci (2011) 61:443–444
DOI 10.1007/s12576-011-0161-z

LETTER TO THE EDITOR

Gene profiling in ductus arteriosus and aorta: a question of consistency

Flavio Coceani · Francesca Scebba · Debora Angeloni

Received: 9 May 2011 / Accepted: 18 June 2011 / Published online: 9 July 2011

In their paper, Jin et al. [1] report findings that are at variance with the gene profile of our earlier work [2]. Specifically, they highlight a difference in the relative expression of certain sarcomeric genes (i.e., *Myl2* and *Myh7*), with the fetal aorta being a dominant site in their study as opposed to the fetal ductus arteriosus in ours, and also note the absence in our data of a host of genes, including those encoding qualifying constituents of constrictor (i.e., endothelin-1) and dilator (i.e., prostaglandin E receptor subtype EP_4) mechanisms in the ductus. However, the two studies, although sharing methodology, are hardly comparable in the analysis of data and finality. While Jin et al. [1] addressed the issue of the relative predominance of transcripts in the ductus versus the aorta antenatally, our aim was to ascertain changes in either vessel linked to birth and oxygen action [2]. Hence, the question of predominance was viewed in a composite perspective in which the terms of reference for the comparison were not limited to the vessel type but also encompassed pre- and postnatal conditions. Nevertheless, from our analysis there emerged the forementioned clustering of cardiac-type sarcomeric genes in the ductus rather than in the aorta. A possible explanation for this apparent inconsistency may be found in the very nature of such transcripts since they are likely to embody, as also implied by Jin et al. [1], a latent potential for maturation of muscle cells to an alternative phenotype. If so, it is not too far-fetched to think that the different strains of rats employed by Jin et al. (Wistar) and ourselves (Long-Evans) may not express this potential with the same distribution pattern; hence, the cause of the observed difference. A question, then, remains on our failure to detect certain transcripts. The situation, one should add, is not unique since the transcriptional profile obtained by Jin et al. [1] is also missing many of the elements seen by us [2]. Noteworthy in the latter respect are transcripts encoding RhoB protein and 12(S)-lipoxygenase in view of their assigned role in ductal control [3, 4]. The reason for any such divergence is found, in our opinion, in an intrinsic limitation of the microarray analysis which, by employing an appropriately high cutoff level to avoid spurious signals, may overlook certain genes, even important ones. Exemplary in this connection is the endothelin-1 transcript which we failed to see by microarray [2] and detected instead by real-time PCR [5]. Our microarray analysis, on the other hand, revealed changes, such as upregulation of the transcription factor Gata2 and downregulation of the endothelin-1 ET_B receptor, indicating an enhanced contractile function of the peptide. In summary, one may conclude that, in comparing transcriptional profiles by the microarray technique, differences are unavoidable and that any such comparison should consider cohort of genes for distinct functions or mechanisms rather than single genes. A final comment is due on the gestation age of the fetuses employed by us (19 days) [2], which is regarded as preterm by Jin et al. [1] vis-à-vis their term group (21 days). In actual fact, the age of our animals fell anywhere between 19 and 20 days, and attempts to postpone the experiment by 1 day was unrewarding due to the high incidence of spontaneous deliveries. The latter finding reaffirms the concept of differences among rat strains.

F. Coceani (✉) · F. Scebba · D. Angeloni
Scuola Superiore Sant'Anna,
Pisa, Italy
e-mail: coceani@sssup.it

References

1. Jin M-H, Yokoyama U, Sato Y, Shioda A, Jiao Q, Ishikawa Y, Minamisawa S (2011) DNA microarray profiling identified a new role of growth hormone in vascular remodelling of rat ductus arteriosus. J Physiol Sci 61:167–179
2. Costa M, Barogi S, Socci ND, Angeloni D, Maffei M, Baragatti B, Chiellini C, Grasso E, Coceani F (2006) Gene expression in ductus arteriosus and aorta: comparison of birth and oxygen effects. Physiol Genomics 25:250–262
3. Kajimoto H, Hashimoto K, Bonnet SN, Haromy A, Harry G, Moudgil R, Nakanishi T, Rebeyka I, Thébaud B, Michelakis ED, Archer SL (2007) Oxygen activates the Rho/Rho kinase pathway and induces RhoB and ROCK-1 expression in human and rabbit ductus arteriosus by increasing mitochondria-derived reactive oxygen species. A newly recognized mechanism for sustaining ductal constriction. Circulation 115:1777–1788
4. Baragatti B, Coceani F (2011) Arachidonate epoxygenase and 12(S)-lipoxygenase: evidence of their concerted involvement in ductus arteriosus constriction to oxygen. Can J Physiol Pharmacol 89:329–334
5. Baragatti B, Ciofini E, Scebba F, Angeloni D, Sodini D, Luin S, Ratto GM, Ottaviano V, Pagni E, Paolicchi A, Nencioni S, Coceani F (2011) Cytochrome *P*-450 3A13 and endothelin jointly mediate ductus arteriosus constriction to oxygen. Am J Physiol Heart Circ Physiol 300:H892–H901