Reviewer's report

Title: Increased vascular endothelin type B and angiotensin type 1 receptors in patients with ischemic heart disease

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Reviewer: M Wendel

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The study by Dimitrijevic and coworkers investigates the distribution of endothelin and angiotensin receptors in subcutaneous resistance vessels of patients with ischemic heart disease. They employed immunofluorescence microscopy and quantified fluorescence intensities in two patient groups with ischemic heart disease compared to healthy controls.

They show that the protein expression of ETB-receptors and AT1-receptors is induced in smooth muscle cells of subcutaneous resistance vessels in patients with ischemic heart disease while ETA- and AT2-receptors were unchanged.

These observations are of interest and are in line with available data in the literature showing that both the endothelin and the angiotensin system are activated and play important pathophysiological roles in atherosclerosis, ischemic heart disease and consecutive heart failure. They also agree with observations from animal experimental and human studies demonstrating that the contribution of the ETB-receptor subtype to ET-1-induced vasoconstriction is enhanced in congestive heart failure.

Major comments:

1. Concerning the methodology employed by the authors
   - The specificity of the antibodies has to be demonstrated either by performing western blots or by pre-absorption experiments with the respective antigens
   - The quantification based on immunofluorescence measurements should be confirmed by western blot analysis. The analysis of mRNA expression would further add valuable information.

2. Concerning the data presentation
   - It is not clear in which terms the groups of patients with angina pectoris and patients undergoing CABG differ. Did all patients in the CABG group have a history of myocardial infarction? What was the time interval between myocardial infarction and CABG? Do the patient groups differ in the clinical degree of severity of heart failure (NYHA classification)? At which time point were NT pro-BNP levels obtained?

3. Were the levels of ET- and AT-receptor expression influenced by drug treatment especially with ACE-inhibitors or AT-blockers?
Minor comments:

1. Reference 11 does not relate to ETB-receptors
2. The authors should include more citations of previous work in the field (for example: Kobayashi et al., 2000; Babaei et al., 2000; Pernow et al., 2000; Böhm et al., 2002; Strachan et al., 2000; Spieker et al., 2001; Cowburn et al., 1999)

Recommendation for publication

Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest

An article of importance in its field

Conflict of interest

I have no conflict of interest to declare