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GATA4 as Candidate Gene for Pericardial Defects

To the Editor:

The interesting article by Drury and colleagues [1] reports a patient with primum atrial septal defect with partial left pericardial defect and discusses the mechanisms of pericardial defect development.

The embryological mechanisms of pericardial development were correctly reported in this article in agreement with the recent literature [2]. However, the genetic causes of normal and abnormal development of the pericardium are still largely unknown.

A recent article reports the impaired mesenchymal cell function in GATA4 gene mutant mice leading to diaphragmatic hernia and heart, pericardial and lung defects [3]. GATA4 is a very important gene for the development of the heart, which is involved in the pathogenesis of familial atrial septal defect [4, 5], and it is the candidate gene for deletion 8p syndrome [6].

Among the heart defect associated with deletion 8p syndrome, we reported a patient with ostium secundum atrial septal defect with partial pericardial defect [7]; it is interesting to note the high frequency of atrial septal defect in this syndrome [7] and in patients with nonsyndromic pericardial defects [1]. In conclusion, we suggest that GATA4 gene should be considered a candidate gene for pericardial defects in humans based on the report in mice [3].

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Reply

To the Editor:

We thank the authors [1] for their helpful comments, regarding our article [2], and suggestion of GATA4 as a candidate gene for pericardial defect in humans.

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Decreasing the Expression of LFA-1 and ICAM-1 as Well as Hindering Their Interaction as the Major Mechanism for Statin-Induced Neutrophil Dysfunction

To the Editor:

I read with great interest the article by Chello and colleagues [1].

This work shows that simvastatin markedly suppresses the functional activity of neutrophils, which is underscored by reduced expression of CD11b ($p < 0.01$ at 24 hours) and a significantly less percentage of cells positive for nitro-blue tetrazolium ($p < 0.01$ at 12 and 24 hours) compared with a placebo. I would like to complement the discussion of Chello and coworkers [1] by introducing a major route through which statins could suppress the activity of neutrophils.

The most important adhesion protein identified on neutrophils is the integrin lymphocyte function-associated antigen-1 (LFA-1; CD11a/CD18), which is the ligand for intercellular adhesion molecule-1 (ICAM-1) expressed on the endothelium. The LFA-1/ICAM-1 interaction is crucial for the ingress of neutrophils into the inflammatory sites [2]. Statins downregulate the expression of ICAM-1 and LFA-1, and through binding to LFA-1, they interfere with ICAM-1–LFA-1 interaction [3]. This important mechanism should be borne in mind as the major mechanism for statin-induced inhibition of neutrophil activity.

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