

## Histogenesis of cardiac myxoma: the potential role of the cardiac neural crest

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Cardiac myxoma is the most common tumor of the heart. The myxoma arises in the region of the interatrial septum and the fossa ovalis, with the left atrium as the most common site of growth. The histogenesis of cardiac myxoma remains unclear. We have previously suggested that a clearer understanding of tumor origins can be achieved through a detailed investigation of heart development (1). In the heart, cardiac neural crest contributes to the septation of the outflow tract, the morphogenesis of the great arteries, and the maturation of the atrioventricular valves and the conduction system (2). We hypothesized that myxoma develops from resident cardiac neural crest cells, via a re-activation of the developmental programs that govern epithelial-mesenchymal transition. Immunohistochemical analysis for canonical markers calretinin, vimentin,  $\alpha$ -SMA, CD31, CD34, S100, plus cardiac neural crest markers plexin A2 and semaphorin 3C was performed in one case of sporadic cardiac myxoma. Primary myxoma cell culture was obtained *ex vivo* via both single cell isolation and outgrowth methods. *In vitro* confocal microscopy confirms the presence of myxoma cells positive for calretinin, vimentin,  $\alpha$ -SMA, CD31, CD34, S100, plexin A2 and semaphorin 3C. Expression of semaphorin 3C and plexin A2 was also confirmed by Western blot analysis. In order to characterize *in vivo* behaviour of cultured myxoma cells,  $2,3 \times 10^6$  cells (cell culture passage 3) were subcutaneously inoculated in interscapular region of immunocompromised mouse. Newly formed tissue was processed for histological and immunohistochemical evaluations. Hematoxylin and eosin staining confirmed the myxoid background of the mass. Despite the presence of CD31-positive human cells, there was no evidence of neovascularization. Our preliminary findings confirm our hypothesis, suggesting that cardiac neural crest in adult heart could be involved in the pathogenesis of cardiac myxoma.

### References

- [1] Di Vito et al. (2015) The mysterious pathways of cardiac myxomas: a review of histogenesis, pathogenesis and pathology. *Histopathology* 66(3):321-32. doi: 10.1111/his.12531.
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### Keywords

Cardiac myxoma; cardiac neural crest; plexinA2; semaphorin3C.