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High frequency of mesenchymal progenitors and osteoprogenitors in the porcine aortic valve

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Objectives:

Advanced valvular lesions often contain mesenchymal tissues that may be elaborated by an unidentified multipotent progenitor subpopulation within the valve interstitium. The objectives of this study were: 1) to test the multi-lineage potential of porcine aortic valve interstitial cells (VICs); and 2) to identify and measure the frequency of the mesenchymal progenitors and osteoprogenitors in freshly isolated and subcultured VICs.

Method:

VICs were cultured in different induction media to test differentiation capacity. The frequency of mesenchymal progenitors and osteoprogenitors were measured using colony forming unit-fibroblast (CFU-F) and colony forming unit-osteoblast (CFU-O) assays, respectively. The osteogenic potential and self-renewal of osteoprogenitors were also tested from single cells.

Results:

We found VICs were inducible to osteogenic, adipogenic, chondrogenic, and myofibrogenic lineages. Primary VICs had strikingly high frequencies of mesenchymal progenitors ($48.0 \pm 5.7\%$) and osteoprogenitors ($44.1 \pm 12.0\%$). High frequencies were maintained for up to six population doublings but decreased after nine population doublings to $28.2 \pm 9.9\%$ and $5.8 \pm 1.3\%$ for mesenchymal progenitors and osteoprogenitors, respectively. We further identified the putative progenitor subpopulation as morphologically-distinct cells that are highly enriched for osteoprogenitors, occur at high frequency, self-renew, and elaborate bone matrix from single cells.

Conclusions:

These novel findings suggest that the aortic valve is rich in a unique multipotent mesenchymal progenitor cell population that is distinct from other vascular progenitor cells. The high frequency of the osteoprogenitors in the aortic valve might have significant implications for the pathobiology of aortic valve calcification.