Aging' Granular Cells in Ameloblastoma have a CD44+/Snail+ Phenotype

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THE PROBLEM
Ameloblastoma, the most clinically significant odontogenic epithelial tumor, is benign but locally-infiltrative. It causes massive jawbone destruction, and local recurrences after treatment. The granular cell ameloblastoma is a rare variant of this neoplasm. The presence of these granular cells have been attributed to aging or degenerative changes.

THE RESEARCH QUESTIONS
- Do 'aging' granular cells in ameloblastoma express cytokines including cancer stem cell (CSC) proteins and epithelial-to-mesenchymal transition transcription factors?
- How important are these cytokines in terms of defining immunophenotypic characteristics and clarifying biological status of these granular cells?

THE RESULTS and DISCUSSION

HISTOLOGY OF GRANULAR CELLS:

Fig. 2. Representative sections of a granular cell ameloblastoma showing granular cells identified as large polygonal cells with abundant eosinophilic granules in their cytoplasm (2A-2C) (Original magnification 2A x 40; 2B x 100; 2C x 400).

EMT EXPRESSIONS:

Fig. 5. Snail intranuclear expression in granular (5A) and non-granular cells (5B) (Original magnification 5A x 200; 5B x 100).

CANCER STEM CELL EXPRESSIONS:

Fig. 3 and 4. Representative sections of ameloblastoma tumor epithelium showing differential immunoreactivity of granular (3A, 3C, 4A, 4C) and non-granular cells (3B, 3D, 4B, 4D) for two cancer stem cell proteins CD44 (3A-D) and ABCG2 (4A-D). (Original magnification 3A, 3B, 3C x 40; 3D x 100; 4C X200; 3C x 400). Adjoining tables detail the subcellular localization and staining intensity levels of these proteins.

Granular cell metaplasia in ameloblastoma may involve the peripheral pre-ameloblast-like cells and/or stellate reticulum-like cells. Microscopically these cells are identified as large polygonal cells with abundant eosinophilic granules in their cytoplasm (Fig. 2A-C).

CD44, a CSC marker and promoter of tumour invasion and metastasis, is detected in the membrane and cytoplasm of granular cells (Fig 3A), thus suggesting that these cells possess CSC characteristics and participate in tumor-induced biological activities. The other CSC markers (ABCG2, CD133 and Bmi-1) were not detected (Fig. 4A-C).

Snail, an EMT inducer and functionally active in its intranuclear position, is detected in the nucleus of the granular cells, thus providing evidence that Snail intranuclear accumulations in these cells support their active roles in EMT (Fig. 5A).

FUTURE WORK:
The next step would be to develop an in vitro model to study ameloblastoma granular cells in primary cultures.

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