IDENTIFICATION OF CANDIDATE GENES FOR GRANULOSA CELL TUMOR PROGRESSION

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BACKGROUND: Granulosa cell tumours (GCTs) are frequently seen in menopausal women and are relatively indolent. Although approximately 80% of patients with advanced tumors die from recurrence, but little is known about the molecular mechanisms of GCT progression. Previously, we characterise the unique properties of a granulosa tumour cell line, KGN cells, for the molecular analysis of GCT progression. KGN cells retain several properties of normal granulosa cells, and acquire an aggressive tumor phenotype *in vitro*. Thus, we adopt this cell line as a model for analyzing GCT progression. In this study, we searched for candidate genes based on the expression level, and the selected genes were employed for functional analysis.

METHODS: Expression analysis using total RNA from normal granulosa cells and KGN cells was carried out Affymetrix Human Genome U133 Plus 2.0 arrays containing 54,120 probe sets (Affymetrix Inc.). Moreover, the expression level of candidate genes in granulosa cell tumor sample and KGN cells at different passages were then determined by RT-PCR, western blot analysis and mmunofluorescence. Finally, selected genes were employed for functional analysis using cells carrying an shRNA gene knockdown construct.

RESULTS: Focusing on the genes highly expressed in KGN cells, 9 genes were selected throughout screening based on distinct properties of KGN cells at different passages. Of these, GPRC5B was highly expressed in KGN cells and human GCT by immunofluorescence and western blot analyses. In the cells carrying a GPRC5B knockdown construct (del GPR cells), more obvious stress fiber was formed compared with the control cells, and the number of cells with nuclear localized β-catenin was significantly lower.

CONCLUSION: These results strongly suggest that GPRC5B is involved in etiology and progression of GCT.