

What pituitary tumours may tell us about the biology of other cancers

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(Medical Xpress) -- Expression levels of a DNA repair gene called MGMT have been widely studied across many cancers as a biomarker of response to temozolomide, a chemotherapeutic agent. Now Australian scientists have published findings suggesting MGMT may also play a significant role in tumour progression.

Previous work by the same group showed that MGMT was expressed at different levels in pituitary tumours, those with low levels being more aggressive. It is those more aggressive tumours that tend to respond to chemotherapy, because MGMT can no longer undo the damage caused by the drug.

The current study looked closely at 19 pituitary tumours, 12 expressing high levels of MGMT, 7 low, showing very different [gene expression profiles](#) between the two groups.

Further investigation also revealed very different [gene networks](#), or ‘signaling pathways’. The tumours with high MGMT expression showed activation of genes implicated in [chemotherapy](#) resistance. Those with low MGMT expression showed activation of genes involved in DNA damage and repair, as well as genes involved in gene transcription.

These results led to the formulation of a model describing the possible role of MGMT in pituitary tumour progression – and the conclusion that the results may apply to many other cancer types.

Endocrinologist Dr Ann McCormack, now at Sydney's Garvan Institute of Medical Research, undertook much of this work in collaboration with Associate Professor Roderick Clifton-Bligh as part of her doctoral studies at the Kolling Institute of Medical Research. Microarray analysis and Gene Set Enrichment Analysis were done with Dr Warren Kaplan from Garvan. The findings are described in Pituitary, now online.

“Pituitary tumours display a strong tendency towards ‘senescence’, akin to hibernation, and most do not become aggressive or malignant,” said Dr McCormack.

“In a small number of cases, however, the tumours emerge from their senescent state and become aggressive. It is likely that prolonged DNA damage signaling contributes to this progression.”

“This study told us that loss of MGMT expression may contribute to the progressive accumulation of genetic mutations and cellular proliferation that occurs.”

“We feel these results would be of interest to other cancer researchers. There has been substantial literature regarding MGMT as a [biomarker](#) of response to temozolomide, however, this is the first paper to examine the relationship between MGMT and genome-wide gene expression profiles in any tumour type.”

“We believe that as well as being a biomarker of treatment response, MGMT may ultimately serve to reflect tumour biology and act as a prognostic indicator. These are preliminary findings and we now need to validate our results.”

Provided by Garvan Institute of Medical Research

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