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### 1) Background

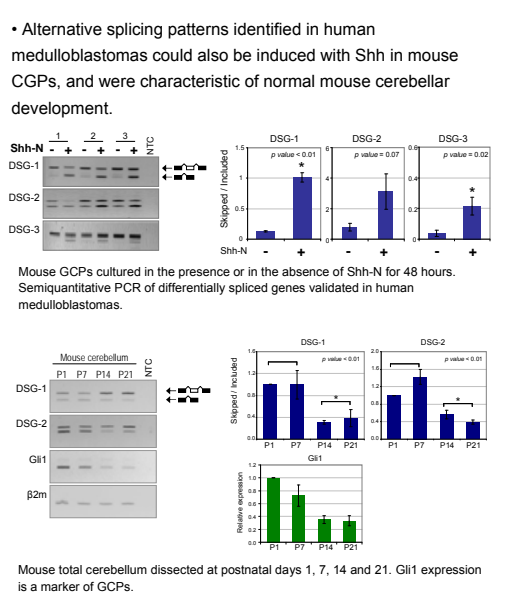
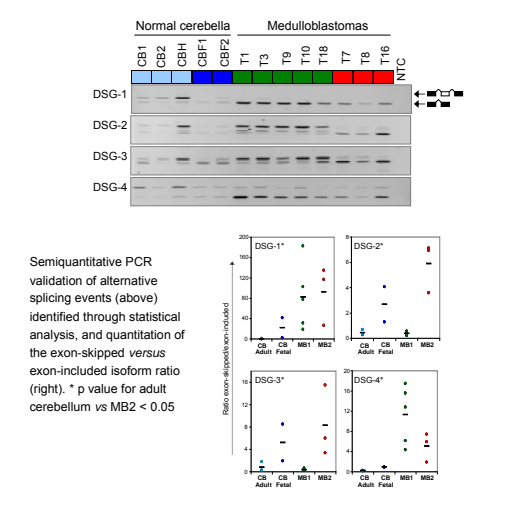
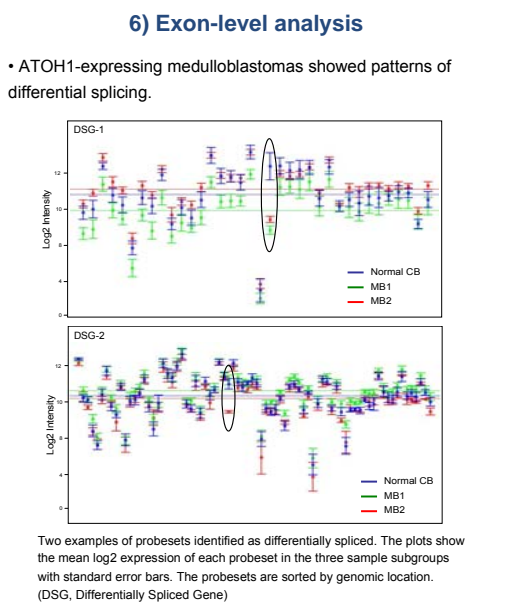
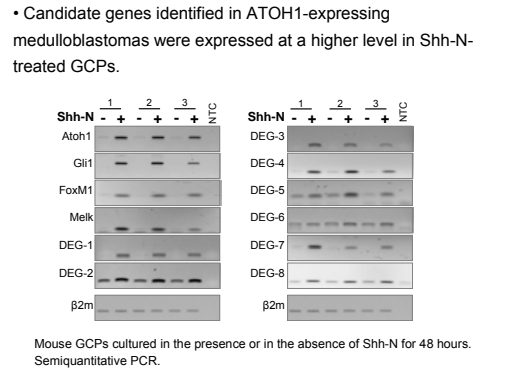
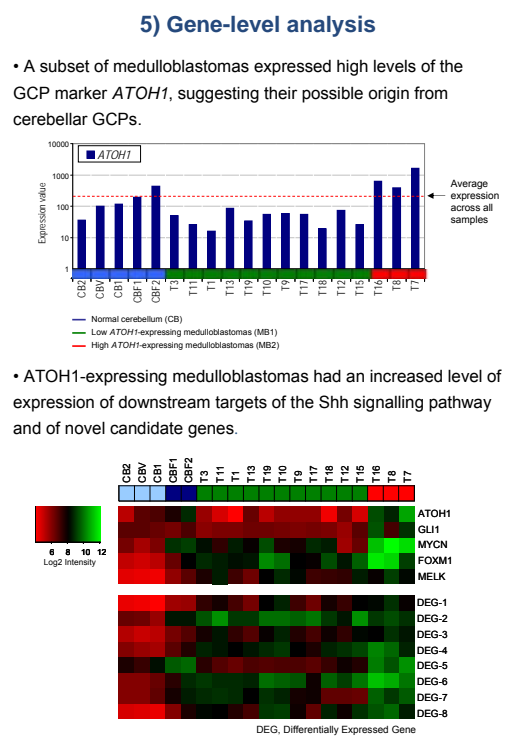
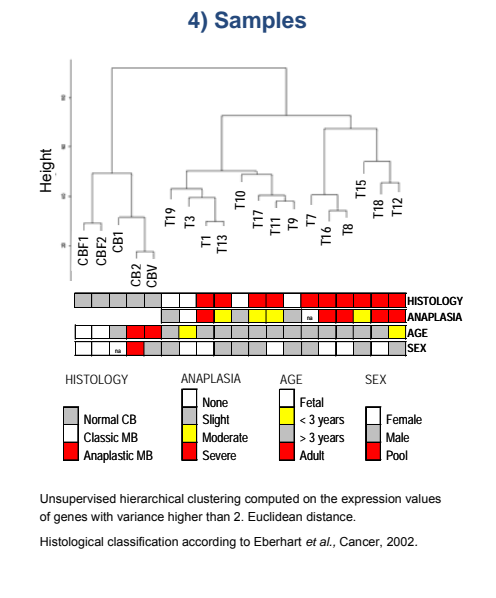
- Medulloblastoma is a malignant tumour of the cerebellum which most commonly affects children.
- A subset of tumours is thought to arise from granule cell progenitors (GCPs) that fail to undergo normal neuronal development, following the hyper-activation of the Sonic Hedgehog (Shh) signalling pathway.

### 2) Aim

To identify candidate genes that may be involved in the regulation of GCP development and malignant transformation.

### 3) Methods

- Affymetrix Exon arrays were used to analyse the transcriptional profiles of 14 medulloblastoma and 5 normal cerebellum samples.
- Statistical analysis identified genes differentially expressed or differentially spliced between normal and tumour samples.
- Candidate genes were validated in primary mouse GCP cultures.



### 7) Conclusions

Exon array analysis identified a subset of human medulloblastomas likely to derive from GCPs. These tumours are characterised by:

- Over-expression of GCP markers and activation of the Shh signalling pathway.
- Differential expression of genes that are upregulated when mouse GCPs are treated with Shh-N *in vitro*.
- Patterns of alternative splicing in common with Shh-N treated mouse GCPs and associated with cerebellar postnatal development.

The candidate genes identified in this study represent interesting targets to investigate the normal development of the cerebellum and the alterations that lead to its malignant transformation.

### Acknowledgements

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