Origin and progression of a neural stem cell tumour in Drosophila.

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Solid neural tumours (e.g. glioblastomas, neuroblastomas) are amongst the deadliest cancers. These tumours are heterogeneous and their growth is sustained by Cancer Stem Cells (CSCs) which exploit self-renewing programs that normal Neural Stem Cells (NSCs) use for tissue development and repair. How tumour-intrinsic factors and microenvironment shape neural tumour progression remains an open question. We have generated a neural stem cell (NSC) derived tumour in Drosophila by aberrant activation of Notch (N) signalling. By genomic approaches, we have shown that N hyperplasia is achieved by activating a network of stemness and growth related transcription factors. The former suppress early differentiation-promoting factors in NSC progeny. These N hyperplasias can be immortalized by serial transplantation in adult hosts. By using transcriptomic, cellular and genetic approaches we have studied the differences between the larval primary N tumour and its more aggressive version, which emerges soon after transplantation to adults. This has provided insights on tumour growth strategies, like the involvement of Myc, the RNA binding protein Imp and the insulin/IGF receptor pathway. We found that host macrophages profusely infiltrate the allografted tumour and impede its growth through phagocytosis. We also found that haemocytes have a pro-tumour role as they may increase the host's morbidity by their propensity to produce damaging extracellular reactive oxygen species. We are currently further investigating the role of intrinsic factors such as the epigenetic regulators E(z) and Mi-2 in N tumour emergence and growth.