Role of the Aurora-A kinase and its regulator TPX2 in control of chromosome stability in human cells

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Research in our lab aims at understanding the mechanisms through which the Aurora-A/TPX2 complex regulates the fidelity of chromosome segregation at mitosis and how altered levels of the complex contribute to tumorigenesis.

Mitotic spindle function regulates chromosome segregation; spindle defects generate genetically unbalanced –aneuploid- daughter cells that may initiate a tumorigenic clone. The mitotic kinase Aurora-A controls bipolar spindle formation and function; the TPX2 protein regulates Aurora-A stability, activity, and localisation to the spindle. Aurora-A and TPX2 are overexpressed in tumors and we have proposed that overexpression of the whole complex is critical to tumorigenesis.

This PhD project will focus on the investigation of the pro-tumorigenic effects of the single or combined overexpression of Aurora-A and TPX2. We have developed tools to this aim, including non-transformed cell lines stably overexpressing each of them or the whole complex, and mutant versions of the proteins impaired in the interaction. Using a combination of cell biology approaches, especially of microscopy-based techniques, and biochemistry, the mechanisms through which overexpression of Aurora-A, TPX2 or the whole complex drives chromosome mis-segregation and influence the proliferation of aneuploid daughter cells -especially by modulating the p53-mediated response- will be characterised. The study will help clarifying the oncogenic functions of the Aurora-A/TPX2 complex.

Selected publications


