

	<b>Experiment title:</b> <b>Mechanism of Aurora-B activation by INCENP and inhibition by Hesperadin</b>	<b>Experiment number:</b> MX-267 MX-394
<b>Beamline:</b>  ID14-1 ID14-4 ID14-2	<b>Date of experiment:</b> from: 28/07/2004 to: 30/07/2004 from: 25/11/2004 to: 26/11/2004 from: 21/07/2005 to: 22/07/2005	<b>Date of report:</b> 27/07/2005
<b>Shifts:</b> 5	<b>Local contact(s):</b> Raimond RAVELLI, Elspeth GORDON, Rana ROY	<i>Received at ESRF:</i>
<b>Names and affiliations of applicants (* indicates experimentalists):</b>  Fabio Sessa, Marina Mapelli, Cataldo Tarricone and Andrea Musacchio Department of Experimental Oncology, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy		

## Report:

Aurora family serine/threonine kinases control mitotic progression and their deregulation is implicated in tumorigenesis. Aurora-A and Aurora-B, the best-characterized members of mammalian Aurora kinases, are ~60 % identical but bind to unrelated activating subunits. The structure of the complex of Aurora-A with the TPX2 activator has been reported previously. We have now determined the crystal structure of Aurora-B in complex with the IN-box segment of the INCENP activator and with the small molecule inhibitor Hesperadin. Aurora-B/INCENP is remarkably different from Aurora-A/TPX2. INCENP forms a crown around the small lobe of Aurora-B and induces the active conformation of the T-loop allosterically. The structure represents an intermediate state of activation of Aurora-B, in which the Aurora-B C-terminal segment stabilizes an open conformation of the catalytic cleft and a critical ion pair in the kinase active site is impaired. Phosphorylation of two serines in the carboxyl-terminus of INCENP generates the fully active kinase. Recently, we have obtained crystals of the complex of Aurora B with the doubly phosphorylated form of INCENP. Structure determination is underway.

## References

Sessa F, Mapelli M, Ciferri C, Tarricone C, Areces LB, Schneider TR, Stukenberg PT and Musacchio A (2005) Mechanism of Aurora-B activation by INCENP and inhibition by Hesperadin, *Mol. Cell* **18**, 379-391.