X	**Experiment title:** **Mechanism of Aurora-B activation by INCENP and inhibition by Hesperadin**	**Experiment number**: MX-267 MX-394
Beamline: ID14-1 ID14-4 ID14-2	**Date of experiment:** from: 28/07/2004 to: 30/07/2004 from: 25/11/2004 to: 26/11/2004 from: 21/07/2005 to: 22/07/2005	**Date of report**: 27/07/2005
Shifts: 5	**Local contact(s)**: Raimond RAVELLI, Elspeth GORDON, Rana ROY	*Received at ESRF:*

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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 phosphoryalated 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.