Protein Kinase Inhibition and Substrate Recognition

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Protein kinases are key components of cell signalling pathways. Defects in these processes lead to diseases such as cancer, diabetes and arthritis and hence protein kinases have become targets for drug design and therapy. We recently reviewed progress in this field with reference to kinase inhibitors that are in clinical trials or in the clinic and for which structural information is available [1]. In this talk I shall review some of our work with reference to cell cycle protein kinases [2] and I shall expand the discussion to consider wider aspects of substrate recognition with reference to CDK2/cyclin A, CDK2/cyclin E [3], CDK7 [4] and polo-like kinase [5].

[1] Noble M.E., Endicott J.A., Johnson L.N., *Science*, 2004, **303**, 1800. [2] Davies T.G., Bentley J. et al., *Nature Structural Biology*, 2002, **9**, 745. [3] Honda R., Lowe E.D., Dubinina E., Skamnaki V., Cook A., Brown N.R., Johnson L.N., *EMBO J.*, 2005, **24**, 452. [4] Lolli G., Lowe E.D., Brown N.R., Johnson L.N., *Structure (Camb)*, 2004, **12**, 2067. [5] Cheng K.-Y., Lowe E.D., Sinclair J., Nigg E.A., Johnson L.N., *EMBO J.*, 2003, **22**, 5757.

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