

7.61 FALL 2006 RECEPTORS & SIGNAL TRANSDUCTION PART 2

Background reading for Lectures 4, 5 and 6 (October 2, 16 and 23).

Please read these before class

These two lectures and the **associated discussion sections (October 17, 26 and November 2)** will cover various types of receptor signaling systems and pathways.

Alberts IV Chapter 15 - especially pages 871-900.

OR

Lodish et al VChapter 14

Some of this material has already been covered in the lectures on receptors and G proteins.

General

Current Opinion in Cell Biology – the second issue each year covers signaling

Hunter, T. (2000). Signaling – 2000 and beyond. Cell 100: 113-127

An excellent overview of the past, present and future of signal transduction.

Receptor Tyrosine Kinases

Schlessinger, J. (2000) Cell signalling by receptor tyrosine kinases. Cell 103: 211-225.
Reviews the evidence for receptor dimerization and activation and for recruitment of signaling molecules – excellent summary.

Schlessinger, J. (2002). Ligand-induced, receptor-mediated dimerization and activation of EGF receptor. Cell 110: 669-672.

Discusses the crystal structures of EGFR/EGF and EGFR/TGF- α and cites earlier work on the structures of other receptors receptors in complex with their ligands.

Cho, H.S., Mason, K., Ramyar, K.X., Stanley, A.M., Gabelli, S.B., Denney, D.W., Jr., and Leahy, D.J. (2003). Structure of the extracellular region of HER2 alone and in complex with the Herceptin Fab. *Nature* 421, 756-760.

Van der Geer, P., Hunter, T. and Lindberg, R.A. (1994). Receptor Protein-tyrosine kinases and their signal transduction pathways. *Annu. Rev. Cell Biol.* 10:251-337.

Thomas, S.M. and Brugge, J.S. (1997) Cellular Functions Regulated by *src* Family Kinases. *Annu. Rev. Cell Dev. Biol.* 13: 513-609.

Heldin, C-H., Ostman, A. and Ronnstrand, L. (1998). Signal transduction via platelet-derived growth factor receptors. *BBA Reviews on Cancer* 1378: F79-F113.

Yarden, Y. 2001. The EGFR family and its ligands in human cancer. signalling mechanisms and therapeutic opportunities. *Eur J Cancer.* 37 Suppl 4:S3-8.

Kullander, K., and Klein, R. (2002). Mechanisms and functions of Eph and ephrin signalling. *Nat Rev Mol Cell Biol* 3, 475-486.

Wells, A., and Marti, U. (2002). Signalling shortcuts: cell-surface receptors in the nucleus? *Nat Rev Mol Cell Biol* 3, 697-702.

Carpenter, G. (2003). Nuclear localization and possible functions of receptor tyrosine kinases. *Curr Opin Cell Biol* 15, 143-148.

Insulin Receptor and its Substrate

McKern et al. (2006) Structure of the insulin receptor ectodomain reveals a folded-over conformation. *Nature* 443: 218-221.

Waters, S.B. and Pessin, J.E. (1996). Insulin receptor substrate 1 and 2 (IRS1 and IRS2): what a tangled web we weave. *Trends Cell Biol.* 6:1-4.

Myers, M.G., Sun, X.J. and White, M.F. (1994). The IRS-1 signaling system. *Trends Biol. Sci.* 19:289-293.

Keller, S.R. and Lienhard, G.E. (1994). Insulin signalling: the role of insulin receptor substrate-1. *Trends Cell Biol.* 4:115-119.

Strålfors, P. (1997). Insulin second messengers. *BioEssays* 19:327-335.

B and T Cell Receptor Complexes

Qian, D. and Weiss, A. (1997). T cell antigen receptor signal transduction. *Curr. Opin. Cell Biol.* 9:205-212.

DeFranco, A. (1993). Structure and function of the B cell antigen receptor. *Annu. Rev. Cell Biol.* 9:377-410.

Crabtree, G.R. and Clipstone, N.A. (1994). Signal transmission between the plasma membrane and nucleus of T lymphocytes. *Annu. Rev. Biochem.* 63:1045-1083.

Cytokine Receptors and Signalling

Ozaki, K., and W.J. Leonard. 2002. Cytokine and cytokine receptor pleiotropy and redundancy. *J Biol Chem.* 277:29355-8.

O'Shea, J.J., M. Gadina, and R.D. Schreiber. 2002. Cytokine signaling in 2002: new surprises in the Jak/Stat pathway. *Cell.* 109 Suppl:S121-31.

Watowich et al. (1996). Cytokine receptor signal transduction and the control of hematopoietic cell development. *Annu. Rev. Cell Dev. Biol.* 12:91-128.

Schindler, C. and Darnell, J.E. (1995). Transcriptional responses to polypeptide ligands: the JAK-STAT pathway. *Annu. Rev. Biochem.* 64:621-651.

Ihle, J.N. (1995). Cytokine receptor signalling. *Nature* 377:591-594.

Darnell, J.E., Ker, I.M. and Stark, G.R. (1994). JAK-STAT pathways and transcriptional activation in response to IFNs and other signalling proteins. *Science* 264:1415-1421.

Taniguchi, T. (1995). Cytokine signalling through nonreceptor protein tyrosine kinases. *Science* 268:251-255.

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Brivanlou, A.H., and Darnell, J.E., Jr. (2002). Signal transduction and the control of gene expression. *Science* 295, 813-818.

TGF β -Receptors and Signalling

Shi and Massague (2003) Mechanisms of TGF- β signaling from cell membrane to nucleus *Cell* 113:685-700.

Massagué, J., Bkain, S.W. and Lo, R.S. (2000) TGF- β signaling in growth control, cancer and heritable disorders. *Cell* 103: 295-309.

Massagué, J. (2000). How cells read TGF β signals. *Nat. Rev. Mol. Cell Biol.* 1: 169-178.

Alevizopoulos, A. and Mermoud, N. (1997). Transforming growth factor- β : the breaking open of a black box. *BioEssays* 19:581-591.

Tyrosine Phosphatases

Hermiston et al. (2002) Reciprocal regulation of lymphocyte activation by tyrosine kinases and phosphatases. *J. Clin. Invest.* 109: 9-14.

Billadeau and Liebson (2002) ITAMs versus ITIMs: striking a balance during cell regulation. *J. Clin. Invest.* 109: 161-167.

Charbonneau, H. and Tonks, N.K. (1992). 1002 Protein phosphatases. *Annu. Rev. Cell Biol.* 8:463-494.

Frearson, J.A. and Alexander, D.R. (1997). The role of phosphotyrosine phosphatases in hematopoietic cell signal transduction. *BioEssays* 19:417-427.

Biwes et al (1996) Structural basis for inhibition of receptor protein-tyrosine phosphatase-a by dimerization. *Nature* 382: 555- 559.

Jiang et al. (1999) Dimerization inhibits the activity of receptor-like protein-tyrosine phosphatase-a. *Nature* 401: 606-610.

Receptor Downregulation

Thien CBF and Langdon WY (2001) Cbl: many adaptations to regulate protein tyrosine kinases. Nature Rev Mol Cell Biol. 2: 294-305.

PI3 Kinases

Czech, M.P. (2000) PIP2 and PIP3: complex roles at the cell surface. *Cell* 100: 603-606.

Rameh, L.E. and Cantley, L.C. (1999). The role of phosphoinositide-3-kinase lipid products in cell function. *J.Biol.Chem.* 274: 8347-8350.

Carpenter, C.L. and Cantley, L.C. (1996). Phosphoinositide kinases. *Curr. Opin. Cell Biol.* 8:153-158.

Toker, A. and Cantley, L.C. (1997). Signalling through the lipid products of phosphoinositide-3-OH kinase. *Nature* 387:673-676.

Franke, T.F., Kaplan, D.R. and Cantley, L.C. (1997). PI3K: Downstream AKTion blocks apoptosis. *Cell* 88:435-437.

Hemmings, B.A. (1997). Akt signaling: Linking membrane events to life and death decisions. *Science* 275:628-630.

Scheid, M.P., and Woodgett, J.R. (2001). PKB/AKT: functional insights from genetic models. *Nat Rev Mol Cell Biol* 2, 760-768.

PROTEIN-PROTEIN INTERACTION DOMAINS

SH2 and SH3 Domains

Pawson, T., and Nash, P. (2003). Assembly of cell regulatory systems through protein interaction domains. *Science* 300, 445-452.

Pawson, T. (1995). Protein modules and signalling networks. *Nature* 373:573-580.

Pawson, T. and Scott, J.D. (1997) Signaling through scaffold, anchoring and adaptor proteins. *Science* 278: 2075-2080.

Cohen, G.B., Ren, R. and Baltimore, D. (1995). Modular binding domains in signal transduction proteins. *Cell* 80:237-248.

Koch, C.A., Anderson, D., Moran, M.F., Ellis, C. and Pawson, T. (1991). SH2 and SH3 domains: elements that control interactions of cytoplasmic signaling proteins. *Science* 252:668-674.

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Schaffhausen, B. and Cantley, L.C. (1993). SH2 domains recognize specific phosphopeptide sequences. *Cell* 72:767-778.

PH Domains

Shaw, G. (1996). The pleckstrin homology domain: an intriguing multifunctional protein module. *BioEssays* 18:35-46.

PTB/PDZ Structures

Harrison, S.C. (1996). Peptide-Surface Association: the case of PDZ and PTB domains. *Cell* 86:341-343.

PDZ Domains

Fanning, A.S. and Anderson, J.M. (1996). Protein-protein interactions: PDZ domain networks. *Curr. Biol.* 6:1385-1388.

Songyang, et al. (1997). Recognition of unique carboxyl-terminal motifs by distinct PDZ domains. *Science* 275:73-77.

Saras, J. and Heldin, C-H. (1996). PDZ domains bind carboxy-terminal sequences of target proteins. *Trends in Biological Sciences* 21:455-458.

WW Domains

Sudol, M. (1996). The WW module competes with the SH3 domain? *TIBS* 12:161-163.

WD Domains

Neer, E.J., Schmidt, C.J., Nambudripad, R. and Smith, T.F. (1994). The ancient regulatory-protein family of WD repeat proteins. *Nature* 371:297-300.