LECTURE #8: PHOSPHOPROTEIN PHOSPHATASES

Assigned (Required) Reading is (1) - (4):

•General Background (in your Reader):

(1) Trinkle-Mulcahy L, Lamond AI (2006) Mitotic phosphatases: no longer silent partners. Curr. Opin. Cell Biol. 18: 623-631.

(2) Swingle M, Ni L, Honkanen RE (2007) Small-molecule inhibitors of ser/thr protein phosphatases: specificity, use and common forms of abuse. Methods Mol Biol. 2007;365:23-38.

(3) Tonks NK (2006) Protein tyrosine phosphatases: from genes, to function, to disease. Nature Rev. Mol. Cell Biol. 7: 833-846.

•Paper for Friday Discussion Session (12/14):

(4) Yang J, Roe SM, Prickett TD, Brautigan DL, Barford D (2007) The structure of Tap42/alpha4 reveals a tetratricopeptide repeat-like fold and provides insights into PP2A regulation. Biochemistry 46: 8807-8815.

Phosphoserine/phosphothreonine-specific Phosphoprotein Phosphatases (*General*)—

Shenolikar S (2007) Analysis of protein phosphatases: toolbox for unraveling cell signaling networks. Methods Mol Biol. 365: 1-8.

Sim AT, Ludowyke RI (2002) The complex nature of protein phosphatases. IUBMB Life. 53: 283-286.

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Barford D (1999) Structural studies of reversible protein phosphorylation and protein phosphatases (Colworth Medal Lecture). Biochem. Soc. Trans. 27: 751-66.

Price NE, Mumby MC (1999) Brain protein serine/threonine phosphatases. Curr Opin Neurobiol. 9: 336-342.

Barford D, Das AK, Egloff MP (1998) The structure and mechanism of protein phosphatases: insights into catalysis and regulation. Annu. Rev. Biophys. Biomol. Struct. 27: 133-164.

Brautigan DL (1997) Phosphatases as partners in signaling networks. Adv Second Messenger Phosphoprotein Res. 31: 113-124.

Cohen PT (1997) Novel protein serine/threonine phosphatases: variety is the spice of life. Trends Biochem. Sci. 22: 245-251.

PP1—

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Leach C, Shenolikar S, Brautigan DL (2003) Phosphorylation of PP1 phosphatase inhibitor-2 at centrosomes during mitosis. J Biol Chem. 278: 26015-26020.

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Terry-Lorenzo RT, Elliot E, Weiser DC, Prickett TD, Brautigan DL, Shenolikar S (2002) Neurabins recruit protein phosphatase-1 and inhibitor-2 to the actin cytoskeleton. J. Biol. Chem. 277: 46535-46543.

Aggen JB, Nairn AC, Chamberlin R (2000) Regulation of protein phosphatase-1. Chem Biol. 7: R13-R23.

Hsu JY, Sun ZW, Li X, Reuben M, Tatchell K, Bishop DK, Grushcow JM, Brame CJ, Caldwell JA, Hunt DF, Lin R, Smith MM, Allis CD. (2000) Mitotic phosphorylation of histone H3 is governed by Ipl1/aurora kinase and Glc7/PP1 phosphatase in budding yeast and nematodes. Cell 102: 279-291.

Van Eynde A, Vulsteke V, Beullens M, Boudrez A, Keppens S, Stalmans W, Bollen M. (2000) Nuclear and subnuclear targeting sequences of the protein phosphatase-1 regulator NIPP1. J Cell Sci. 113: 3761-3768.

Shirato H, Shima H, Sakashita G, Nakano T, Ito M, Lee EY, Kikuchi K. (2000) Identification and characterization of a novel protein inhibitor of type 1 protein phosphatase. Biochemistry. 39: 13848-13855.

PP2A—

Janssens V, Goris J, Van Hoof C (2005) PP2A: the expected tumor suppressor. Curr. Opin. Genet. Dev. 15: 34-41.

Van Hoof C, Goris J (2004) PP2A fulfills its promises as tumor suppressor: which subunits are important? Cancer Cell 5: 105-106.

Santhanam A, Hartley A, Duvel K, Broach JR, Garrett S (2004) PP2A phosphatase activity is required for stress and Tor kinase regulation of yeast stress response factor Msn2p. Eukaryot. Cell. 3: 1261-1271.

Zabrocki P, Van Hoof C, Goris J, Thevelein JM, Winderickx J, Wera S (2002) Protein phosphatase 2A on track for nutrient-induced signalling in yeast. Mol Microbiol. 43: 835-842.

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PP2B (calcineurin)—

Cyert MS (2003) Calcineurin signaling in *Saccharomyces cerevisiae*: how yeast go crazy in response to stress. Biochem. Biophys. Res. Commun. 311: 1143-1150.

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PP2C—

Warmka J, Hanneman J, Lee J, Amin D, Ota I (2001) Ptc1, a type 2C Ser/Thr phosphatase, inactivates the HOG pathway by dephosphorylating the mitogen-activated protein kinase Hog1. Mol Cell Biol. 21: 51-60.

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Gaits F, Russell P. (1999) Vacuole fusion regulated by protein phosphatase 2C in fission yeast. Mol Biol Cell 10: 2647-2654.

PP4, PP5, PP6, PPZ, etc.—

Chinkers M (2001) Protein phosphatase 5 in signal transduction. Trends Endocrinol Metab. 12: 28-32.

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<u>Phosphotyrosine-specific Phosphoprotein phosphatases</u>:

Pao LI, Badour K, Siminovitch KA, Neel BG (2007) Non-receptor protein-tyrosine phosphatases in immune cell signaling. Annu. Rev. Immunol. 25: 473-523.

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Cdc25 phosphatase—

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Dual-specificity Phosphoprotein Phosphatases:

MAPK phosphatases—

Theodosiou A, Ashworth A (2002) MAP kinase phosphatases. Genome Biol. 3: Rev. S3009.1-S3009.10.

Keyse SM. (2000) Protein phosphatases and the regulation of mitogen-activated protein kinase signalling. Curr Opin Cell Biol. 12: 186-192.

Pestell KE, Ducruet AP, Wipf P, Lazo JS (2000) Small molecule inhibitors of dual specificity protein phosphatases. Oncogene 19: 6607-6612.

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Cdc14—

Jensen S, Geymonat M, Johnston LH (2002) Mitotic exit: delaying the end without FEAR. Curr Biol. 12: R221-R223.

Li L, Ljungman M, Dixon JE. (2000) The human Cdc14 phosphatases interact with and dephosphorylate the tumor suppressor protein p53. J Biol Chem. 275: 2410-2414.

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PTEN Tumor Suppressor:

Mayo LD, Donner D (2002) The PTEN, Mdm2, p53 tumor suppressor-oncoprotein network. Trends Biochem Sci. 27: 462-467.

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Fcp1 phosphatase—

Kong SE, Kobor MS, Krogan NJ, Somesh BP, Soegaard TM, Greenblatt JF, Svejstrup JQ (2004) Fcp1 phosphatase: Interaction with elongating RNA polymerase II holoenzyme, enzymatic mechanism of action, and genetic interaction with elongator. J. Biol. Chem. 2004 Nov 24 [E-pub ahead of print]

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Eyes-Absent (Eya) phosphatase—

Rayapureddi JP, Hegde RS (2006) Branchio-oto-renal syndrome associated mutations in Eyes Absent-1 result in loss of phosphatase activity. FEBS Lett. 580: 3853-3859.

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Practical matters:

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Dounay AB, Forsyth CJ (2002) Okadaic acid: the archetypal serine/threonine protein phosphatase inhibitor. Curr Med Chem. 9: 1939-1980.

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