

Essentials of Glycobiology (MED 225/CHEM 237/BIOM 222/BGGN 236/CMM 225)

Mondays and Thursdays, 10:30 am- 12:00 pm, Room 1079 CMM-East

Credit: 4 units of credit. Letter grade and S/U grading options available.

Course directors: **Jeffrey D. Esko/Ajit Varki**

Office: 1055 Cellular and Molecular Medicine East Phone: 2-1100 (tough) E-mail: jesko@ucsd.edu (easy)

Administrative Assistance: Barbara Thompson Phone: 2-1101 E-mail: b1thomps@ucsd.edu

The primary aim of the course is to provide an overview of fundamental facts, concepts, and methods in glycobiology. The course is structured around major themes in the field, supported by selected readings from the textbook, "Essentials of Glycobiology" and original literature. Background information will be provided through brief lectures, with detailed discussion of classic or current papers. **Grading is based on regular attendance, class participation, and a take-home written essay on a topical issue in glycobiology.**

The 2nd edition of Essentials of Glycobiology, Varki A, Cummings R, Esko J, Freeze H, Stanley, P., Bertozzi, C., Hart G, and Etzler, M. (editors). 2008 Cold Spring Harbor Laboratory Press, New York is currently in press. Chapters will be available to participants in the course. **BKG Reading and Original Literature are required reading.** Chapters in parentheses are optional, but will embellish the topic.

Lecture	Date	Topic	Discussion Leader(s)	BKG Reading	Original Literature
1	Mar 27	Course Overview History of Glycobiology, Primer on Glycans Lectins, and Biological Functions	Esko/Varki	1,6,(2)	Chapters 1 and 6 provide an overview of glycans, lectins, and biological functions. For further information on glycan structure read Chapter 2.
2	Mar 31	Cellular organization and transferase structure	Paulson (JE)	3,5	Ramakrishnan B, Qasba PK. Role of a single amino acid in the evolution of glycans of invertebrates and vertebrates. J Mol Biol. 2007. 365:570 PMID: 17084860
3	Apr 3	Lectins and principles of glycan recognition	Esko (HF)	26,(27)	Dam TK et al. Binding studies of α -GalNAc-specific lectins to the α -GalNAc (Tn-antigen) form of porcine submaxillary mucin and its smaller fragments. J Biol Chem. 2007. 282:28256. PMID: 17652089. Chapter 27 provides detailed methods and thermodynamic considerations for glycan-protein interactions.
4	Apr 7	Assembly of precursors	Freeze (JE)	4	Niehues R et al. Carbohydrate-deficient glycoprotein syndrome type Ib. Phosphomannose isomerase deficiency and mannose therapy. J Clin Invest. 1998.101:1414 PMID: 9525984
5	Apr 10	N-glycans and Quality Control	Freeze (JE)	8 (36)	Hammond et al. Role of N-linked oligosaccharide recognition, glucose trimming, and calnexin in glycoprotein folding and quality control. Proc Natl Acad Sci U S A. 1994 91:913 PMID: 8302866; (Chp 36 describes the ER quality control system in detail and ERAD).
6	Apr 14	O-glycans and C-type lectins	Esko (HF)	9 (31)	Ju T, Cummings RD. A unique molecular chaperone Cosmc required for activity of the mammalian core 1 β 3-galactosyltransferase. Proc Natl Acad Sci U S A. 2002. 99:16613. PMID: 12464682; Bevilacqua MP et

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					al. Endothelial leukocyte adhesion molecule 1: an inducible receptor for neutrophils related to complement regulatory proteins and lectins. Science. 1989. 243:1160. PMID: 2466335; (Chp 31 describes C-type lectins in detail).
7	Apr 17	Glycosphingolipids and GPI anchors	Esko (HF)	10,11	Optional Reading: Griffiths JS et al. Glycolipids as receptors for Bacillus thuringiensis crystal toxin. Science. 2005. 307:922. PMID: 15705852
8	Apr 21	Proteoglycans, hyaluronan and binding proteins	Esko (PG)	(15),16,35	Kamimura K, et al. Specific and flexible roles of heparan sulfate modifications in Drosophila FGF signaling. J Cell Biol. 2006 174:773. PMID: 16966419; (Chp 15 describes hyaluronan).
9	Apr 24	Glycans and signaling	Gagneux (AV)	37,12 (notch)	Moloney et al. Fringe is a glycosyltransferase that modifies Notch. Nature. 2000. 406:369 PMID 10935626; Brückner K, et al. Glycosyltransferase activity of Fringe modulates Notch-Delta interactions. Nature. 2000 406:411. PMID: 10935637
10	Apr 28	Nuclear and cytoplasmic glycosylation, O-GlcNAc	Varki (JE)	(17),18	Torres, C. R. & Hart, G. W. Topography and polypeptide distribution of terminal N-acetylglucosamine residues on the surfaces of intact lymphocytes. Evidence for O-linked GlcNAc. J. Biol. Chem. 1984. 259:3308 PMID: 6421821; Dentin R, Hedrick S, Xie J, Yates J 3rd, Montminy M. Hepatic glucose sensing via the CREB coactivator CRT2. Science. 2008 Mar 7;319(5868):1402-5. PMID: 18323454 (Chp 17 describes other forms of non-Golgi glycosylation).
11	May 1	Sialic acids and I-type lectins	Varki (JE)	14,32	Crocker PR, et al. Sialoadhesin, a macrophage sialic acid binding receptor for haemopoietic cells with 17 immunoglobulin-like domains. EMBO J. 1994. 13:4490. PMID: 7925291
12	May 5	Galectins	Varki (HF)	(13),33	Lau KS, et al. Complex N-glycan number and degree of branching cooperate to regulate cell proliferation and differentiation. Cell. 2007 129:123. PMID: 17418791; (Chp 13 describes sequences common to different glycan classes).
13	May 8	Lysosomal degradation and P-type lectins	Freeze (AV)	(41),30	Hickman S & Neufeld EF. A hypothesis for I-cell disease: defective hydrolases that do not enter lysosomes. Biochem Biophys Res Commun. 1972. 49:992 PMID: 4345092; (Chp 41 describes genetic disorders of glycan degradation).
14	May 12	Plants and L-type lectins	Varki (JE)	(22),29,45	Mendelsohn J et al. The rapid induction by phytohemagglutinin of increased alpha-aminoisobutyric acid uptake by lymphocytes. J Clin Invest. 1971 50:818. PMID: 4100684; (Chp 22 describes glycans present in green plants).
15	May 15	R-type lectins	Varki (PG)	28	Fiete D, et al. A hepatic reticuloendothelial cell receptor specific for SO4-4GalNAc beta 1,4GlcNAc beta 1,2Man alpha that mediates rapid clearance of lutropin. Cell. 1991 67:1103. PMID: 1662117
16	May 19	Genomics & evolution	Gagneux (AV)	7,19	Galili U & Swanson K. Gene sequences suggest inactivation of α 1,3-galactosyltransferase in catarrhines after the divergence of apes from

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					monkeys. Proc Natl Acad Sci 1991. 88:7401 PMID: 1908095; Martin MJ, et al. Evolution of human-chimpanzee differences in malaria susceptibility: relationship to human genetic loss of N-glycolylneuraminic acid. Proc Natl Acad Sci 2005. 102:12819. PMID: 16126901
17	May 22	Glycan Synthesis, and Glycomics	Bertozzi (AV)		(47),48,49; (Chp 47 covers analysis and sequencing of glycans).
	May 26	Memorial Day – No Class			
18	May 29	Microbial Cell Walls and Colonization	Esko (AV)	20 (21,34)	Bry L, et al. A model of host-microbial interactions in an open mammalian ecosystem. Science. 1996 273:1380. PMID: 8703071; Sonnenburg JL, et al. Glycan foraging in vivo by an intestine-adapted bacterial symbiont. Science. 2005. 307:1955. PMID: 15790854 (Chps 21 and 34 cover Fungi and Microbial adhesins).
19	Jun 2	Microbial infection	Esko (PG)	39 (40)	Kitov PI, et al. Shiga-like toxins are neutralized by tailored multivalent carbohydrate ligands. Nature. 2000 403:669. PMID: 10688205; Kawakubo M, et al. J. Natural antibiotic function of a human gastric mucin against Helicobacter pylori infection. Science. 2004 305:1003. PMID: 15310903; (Chp 40 covers parasitic glycobiology and infection).
20	Jun 5	Glycans in development	Esko (HF)	23 (24,25,38)	Hwang HY, et al. Caenorhabditis elegans early embryogenesis and vulval morphogenesis require chondroitin biosynthesis. Nature. 2003. 423:439. PMID: 12761549; Olson SK, et al. Identification of novel chondroitin proteoglycans in Caenorhabditis elegans: embryonic cell division depends on CPG-1 and CPG-2. J Cell Biol. 2006 173:985. PMID: 16785326; (Chps 24, 25, and 38 cover Arthropods, and glycans in vertebrate development and systemic physiology).
21	Jun 9	Genetic disorders and acquired diseases	Freeze (JE)	42 (43,44,46)	Kornak U. et al. Impaired glycosylation and cutis laxa caused by mutations in the vesicular H ⁺ -ATPase subunit ATP6V0A2. Nat Genet. 2008 40:32 PMID: 18157129; (Chps 43, 44, 46 cover glycans in acquired diseases, cancer, and somatic cell genetics).
22	Jun 12	Inhibitors and pharmaceutical design	Esko	50,51	Platt FM et al. Prevention of lysosomal storage in Tay-Sachs mice treated with N-butyldeoxyojirimycin. Science. 1997 276:428 PMID: 9103204; Miglustat