



11 September, 2000

0499 TO SEP 19 P1:42

Docket No. OON-0930
Dockets Management Branch (HFA-305)
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

I am writing to nominate Dr. Gordon Holt to serve on the FDA's working groups under the Nonclinical Studies Subcommittee of the Advisory Committee for Pharmaceutical Science to identify and report on scientific issues relating to biomarkers of cardiotoxicity and vasculitis. This nomination calls for particular expertise in proteomics and genomics. Dr. Holt has both. Oxford GlycoSciences (OGS) is a world-leader in proteomics, and Dr. Holt plays broad roles in the Company's use of this technology for research, drug discovery and drug development. He currently is engaged in very promising proteomics studies with Frank Sistare (Division of Applied Pharmacology Research, CDER/FDA) to identify biomarkers of drug-induced cardiotoxicity and vasculitis. He also is the Company's principal scientist for a variety of internal and collaborative proteomics projects to identify biomarkers of liver, kidney, cardiac and vascular responses to a wide variety of xenobiotic agents. Finally, he served as a lead scientist in OGS's program with Incyte Genomics (Palo Alto, CA) to develop *LifeExpress*, a combined proteomics-genomics database now marketed to pharma subscribers.

Dr. Holt is a recognized authority on proteomics, having written numerous articles and patent applications on the subject. He also gave invited proteomics lectures at over a dozen major conferences last year alone. Biographical material outlining these activities, as well as describing Dr. Holt's other career milestones is included below.

I have spoken with Dr. Holt about this nomination, and he has agreed to serve on these committees if selected.

Sincerely,

A handwritten signature in black ink, appearing to read 'Martin Page', written over a white background.

Martin Page
Directory of Biology

OON-0930

C2

Gordon D. Holt, PhD

Oxford GlycoSciences

Education:

- **Ph.D.** in Biochemistry, The Johns Hopkins University School of Medicine (1987).
- **B.A.** in Chemistry, Washington University in St. Louis (1982).

Research/Professional Experience:

- 4/1994 - Present **Director of Scientific Development & Principal Scientist**
Oxford GlycoSciences
Gaithersburg, Maryland & Abingdon, Oxfordshire UK
- o Proteomics
 - Principal scientist
 - internal and external programs
 - experimentation, data analysis, patenting
 - o Drug discovery and development
 - Program manager / Principal scientist
 - internal and external programs
 - experimental design, data analysis, patenting
 - o Marketing and business development
 - Public and confidential presentations
 - Document preparation
- 8/1991 - 1994 **Senior Staff Fellow**
with Dr. B. Gahl - Human Genetics Branch
National Institute of Child Health and Human Development
National Institutes of Health, Bethesda, MD
- o Characterized Carbohydrate-Deficient Glycoprotein Syndrome in humans.
- 8/1988 - 1991 **Intramural Research Training Award Fellow & Staff Fellow**
with Dr. V. Ginsburg - Laboratory of Structural Biology
National Institute of Diabetes, Digestive, and Kidney Diseases
National Institutes of Health, Bethesda, MD
- o Identified sulfated carbohydrate-binding domains in proteins and characterized this function in viral and malaria infection, complement fixation and tumor metastasis.
- 7/1983 - 1988 **Post-doctoral Fellow & Graduate Student**
with Dr. G. Hart - Department of Biological Chemistry
The Johns Hopkins University School of Medicine, Baltimore, MD
- o Described OGlcNAc addition on various cytoplasmic and nucleoplasmic glycoproteins.
- 7/1982 - 1983: **Research Assistant II**
with Drs. G. Broze & J. Miletich - Dept of Haematology and Oncology
Washington University School of Medicine, St. Louis MO
- o Developed purification methods for von Willebrand factor, Factor V and Factor XIIIc.

7/1978 - 1982

Research Assistant I with Dr. Philip Stahl
Department of Physiology and Biophysics
Washington University School of Medicine, St. Louis, MO

- Purified and characterized serum mannose binding protein

Grants

- Author and Principal Investigator for the Small Business Innovation Research grant "Development of anti-hepatitis B therapeutics" (DHHS, US Government; 1998).

Patents

- Genetic disease treatments (Application filed)
- Peroxisome proliferation-associated liver proteins (Application filed)
- [Numerous proteomics-based applications for diseases & conditions in preparation]

Honors and Awards:

- Chair, CHI Conference on Functional Genomics (October, 1999)
- Invited book reviewer for *The Quarterly Review of Biology* (1994).
- Chair, Organizing Committee for the conference, "Glycobiology: New Perspectives on Human Disease", National Institutes of Health (1993).
- Technical reviewer for *Alcohol and Glycoconjugates Strategic Planning Session*, National Institute on Alcohol Abuse and Alcoholism (1993).
- Paul Ehrlich Award in Basic Science Research, The Johns Hopkins University School of Medicine (Highest honor conferred to JHUSM PhD graduates; 1987).
- Magna Cum Laude, Washington University in St. Louis (1982).
- Ad hoc grant reviewer, National Science Foundation (1987-1994).
- Ad hoc reviewer: *The Journal of Biological Chemistry*; *Proceedings of the National Academy Sciences, USA*; *Archives of Biochemistry and Biophysics*; *Glycobiology*; *The Glycoconjugate Journal*; *Academic Press, Inc*; *Journal of Cellular Physiology*.

Invited Lectures:

- "Proteomics and safety biomarker discovery;" Nonclinical Studies Subcommittee of the Advisory Committee for Pharmaceutical Science - CDER, FDA (Rockville, MD; March 2000)
- "Combining proteomics and genomics for gene expression analysis;" CHI Conference on Functional Genomics (Boston, MA; October, 1999)
- "Pharmacogenetics, genomic, proteomics: The new frontiers in drug development;" Seventh Human Genome Project: Commercial Implications (San Francisco, CA; February, 2000)
- "Proteomics: Bridging the genomics gap for gene expression analysis;" California Separation Society (Palo Alto, CA; September, 1999)
- "Proteome-based identification of markers for primary hepatocellular carcinoma;" IBC Cancer Marker Conference (San Diego, CA; August, 1999)
- "Integration of proteomics and Genomics for gene Expression Analysis;" Thomas Jefferson University (Doylestown, PA; May, 1999)
- "Proteomic analysis in molecular toxicology;" IBC Molecular Toxicology conference (Washington, D.C.; April, 1999)
- "Proteomic profiling for toxicity assessment and lead prioritization;" Cambridge Healthtech Institute Lead Optimization Conference (San Diego, CA; March, 1999)

- "Use of secreted protein expression analysis to identify molecular markers for improved clinical diagnosis," Cambridge Healthtech Institute Tri-Genome Human Genome Project Conference (San Francisco, CA; February, 1999)
- "Glycotechnology-oriented diagnostics," Massachusetts Institute of Technology; Boston Glycobiology Group (Boston, MA; October, 1996)
- "Trends in glycotechnology-oriented diagnostics: New perspectives on genetic diseases and their implications for therapeutics", Cambridge Healthtech Institute Glycotechnology Conference (San Diego, CA; May, 1995)
- "Building Bridges: Opportunities and Challenges in Forming Academic-Industrial Partnerships", International Perspectives in Glycobiology session of the Second Oxford International Conference, (Oxford, England; September, 1994).
- "Accumulation of Mucin Oligosaccharides in a Patient with Clinical Features of Intracellular Storage", Joint American Pediatric Society/Society for Pediatric Research/ Ambulatory Pediatric Association meeting, (Washington, D.C.; May, 1993).
- "Analysis of the Glycosylation Defect Associated with Carbohydrate-Deficient Glycoprotein Syndrome", Society for Inherited Metabolic Diseases meeting, (Monterey, CA; March, 1993).
- "Carbohydrate-Binding Properties Predicted From Sequence Homologies With Other Lectins. The Case of Malaria Coat Proteins and Sporozoites.", John Radcliffe Hospital, Oxford University, (Oxford, United Kingdom; April, 1992).
- "Malaria Coat Proteins and Sporozoites Bind Sulfated Glycans. Carbohydrate-Binding Properties Predicted From Sequence Homologies With Other Lectins.", Commission of the European Communities Malaria Research Contract Holders Meeting (Orvieto, Italy; April, 1992).
- "Carbohydrate Binding Properties Predicted by the Amino Acid Sequence Homology Identification.", National Institute of Dental Research, NIH (Bethesda, MD; April, 1991).
- "Identifying Carbohydrate Binding Proteins Based on Amino Acid Sequence Homology.", Washington University School of Medicine (St. Louis, MO; August, 1990).
- "Nucleoplasmic and Cytoplasmic Proteins Bear O-GlcNAc moieties.", Society for Complex Carbohydrates Meeting (Bethesda, MD; November, 1987).

Professional Societies:

- The Society for Glycobiology
- The American Society for Cell Biology
- The American Association for the Advancement of Science.

Publications:

1. Stahl, P.D., Holmlund, T., and Holt, G.D. (1982) Strategies for Enzyme Uptake Modification to Facilitate Enzyme Uptake. *Advances in the Treatment of Inborn Errors of Metabolism* (R.W.E. Watts, R.A. Chalmers, M. d'A. Crawford, and D.A. Gibbs, eds.). J. Wiley and Sons, Pub.
2. Konish, M., Shepherd, V., Holt, G.D., and Stahl, P.D. (1983) Uptake of Glycoproteins and Glycoconjugates by Macrophages. *Methods in Enzymology* 98, 301-304.
3. Holt, G.D., Swiedler, S.J., Freed, J.H., and Hart, G.W. (1985) Murine Ia-Associated Invariant Chain's Processing to Complex Oligosaccharide Forms and Its Dissociation From the I-A^k complex. *J. Immunol.* 135, 399-407
4. Holt, G.D., and Hart, G.W. (1986) The Subcellular Distribution of Terminal N-Acetylglucosamine Moieties. Localization of a Novel Protein-Saccharide Linkage, O-Linked GlcNAc. *J. Biol. Chem.* 261, 8049-8057.

5. Holt, G.D., Snow, C.M., Senior, A., Haltiwanger, R.S., Gerace, L., and Hart, G.W. (1987) Nuclear Pore Complex Glycoproteins Contain Cytoplasmically Disposed O-Linked N-Acetylglucosamine. *J. Cell Biol.* 104, 1157-1164.
6. Holt, G.D., Haltiwanger, R.S., Torres, C.-R., and Hart, G.W. (1987) Erythrocytes Contain Cytoplasmic Glycoproteins. O-Linked GlcNAc on Band 4.1. *J. Biol. Chem.* 262, 14847-14850.
7. Hart, G.W., Holt, G.D., and Haltiwanger, R.S. (1990) Nuclear and Cytoplasmic Glycosylation: Novel Saccharide Linkages in Unexpected Places. *Proteins: Form and Function* (R.A. Bradshaw and M. Purton, eds.). Elsevier Science Publishers.
8. Hart, G.W., Haltiwanger, R.S., Holt, G.D., and Kelly, W.G., (1988) Nucleoplasmic and Cytoplasmic Glycoproteins. *Ciba Found. Symp.* 145, 102-118.
9. Hart, G.W., Holt, G.D., and Haltiwanger, R.S. (1988) Nuclear and Cytoplasmic Glycosylation: Novel Saccharide Linkages in Unexpected Places. *Trends Biochem. Sci.* 13, 380-384.
10. D'Onofrio, M., Starr, C.M., Park, M.K., Holt, G.D., Haltiwanger, R.S., Hart, G.W., and Hanover, J.A. (1988) Partial cDNA Sequence Encoding a Nuclear Pore Protein Modified by O-Linked N-Acetylglucosamine. *Proc. Natl. Acad. Sci., USA.* 85, 9595-9599.
11. Hart, G.W., Haltiwanger, R.S., Holt, G.D., and Kelly, W.G., (1989) Glycosylation in the Nucleus and Cytoplasm. *Annu. Rev. Biochem.* 58, 841-874.
12. Whiteheart, S.W., Passaniti, A., Reichner, J.S., Holt, G.D., Haltiwanger, R.S., and Hart, G.W. (1989) Glycosyltransferase Probes. *Methods in Enzymology* 179, 82-95.
13. Haltiwanger, R.S., Holt, G.D., and Hart, G.W. (1990) The Enzymatic Addition of O-N-Acetylglucosamine to Nuclear and Cytoplasmic Proteins. Identification of a Uridine Diphosphate-N-Acetylglucosamine:Peptide β -N-Acetylglucosaminyltransferase. *J. Biol. Chem.* 265, 2563-2568.
14. Holt, G.D., Krivan, H.C., Gasic, G.J., and Ginsburg, V. (1989) Antistasin, an Inhibitor of Coagulation and Metastasis, Binds to Sulfatide [Gal(3-SO₄) β 1-1Cer] and Has a Sequence Homology with Other Proteins That Bind Sulfated Glycoconjugates. *J. Biol. Chem.* 264, 12138-12140.
15. Holt, G.D., Pangburn, M.K., and Ginsburg, V. (1990) Properdin Binds to Sulfatide [Gal(3-SO₄) β 1-1Cer] and Has a Sequence Homology with Other Proteins That Bind Sulfated Glycoconjugates. *J. Biol. Chem.* 265, 2852-2855.
16. Kyogashima, M., Krivan, H.C., Schweinle, J.E., Ginsburg, V., and Holt, G.D. (1990) Glycosphingolipid Binding Specificity of the Mannose-Binding Protein from Human Sera. *Archiv. Biochem. Biophys.* 283, 217-222.
17. Pancake, S.J., Holt, G.D., Mellouk, S., and Hoffman, S.L. (1991) Malaria Sporozoites and Circumsporozoite Proteins Specifically Bind Sulfated Glycoconjugates. *J. Cell. Biol.* 117, 1351-1357.
18. Holt, G.D. (1991) Identifying Glycoconjugate-Binding Domains. Building on the Past. *Glycobiology.* 1, 329-336.
19. Pancake, S.J., Holt, G.D., Mellouk, S., and Hoffman, S.L. (1993) Malaria Sporozoites and Circumsporozoite Protein Bind Sulfated Glycans: Carbohydrate Binding Properties Predicted From Sequence Homologies with Other Lectins. *Parasitologia* 35, 77-80 (suppl.).
20. Krasnewich, D.M., Holt, G.D., Brantly, M., Skovby, F., Redwine, J., Gahl, W.A. (1995) Abnormal synthesis of dolichol-linked oligosaccharides in carbohydrate-deficient glycoprotein syndrome. *Glycobiology* 5, 503-510.
21. Page, M., Moyses, C., Holt, G., Matheson, A. (In Press) Proteomics. Modern Methods of Drug Discovery. (T. Springer, ed)

FedEx

9-18-00

FedEx Tracking Number

820556633260

Form I.D. No.

0200

1 From
Date 9/18/00

Sender's Name Gordon Holt Phone 201 269-5422

Company Oxford Glyco Sciences

Address 4 Spaceman Valley Ct

City Montgomeri Village State MD ZIP 20898

2 Your Internal Billing Reference

3 To
Recipient's Name c/o David Mackey 301-594-5684
Lockett Management Branch Phone 202-277-5182

Company Lockett Management Branch (HFA-765)

Address Fed and Drug Administration

5600 Fishers Lane

City Rockville State MD ZIP 20852



4a Express Package Service

FedEx Priority Overnight Next business morning
 FedEx Standard Overnight Next business afternoon
 FedEx First Overnight Earliest next business morning delivery to select locations
 FedEx 2Day* Second business day
 FedEx Express Saver* Third business day
* FedEx Letter Rate not available Minimum charge. One-pound rate

4b Express Freight Service

FedEx 1Day Freight* Next business day
 FedEx 2Day Freight Second business day
 FedEx 3Day Freight Third business day
* Call for Confirmation

5 Packaging

FedEx Letter*
 FedEx Pak*
 Other Pkg. Includes FedEx Box, FedEx Tube, and customer pkg.
* Declared value limit \$500

6 Special Handling

Saturday Delivery Available for FedEx Priority Overnight and FedEx 2Day to select ZIP codes
 Sunday Delivery Available for FedEx Priority Overnight to select ZIP codes
 HOLD Weekday at FedEx Location Not available with FedEx First Overnight
 HOLD Saturday at FedEx Location Available for FedEx Priority Overnight and FedEx 2Day to select locations

Does this shipment contain dangerous goods?
One box must be checked.
 No
 Yes As per attached Shipper's Declaration
 Yes Shipper's Declaration not required
 Dry Ice Dry Ice, 9, UN 1845 x _____ kg
 Cargo Aircraft Only
Dangerous Goods cannot be shipped in FedEx packaging

7 Payment Bill to:

Enter FedEx Acct. No. or Credit Card No. below.
 Obtain Recip. Acct. No.
 Sender Acct. No. in Section I will be billed
 Recipient
 Third Party
 Credit Card
 Cash/Check

Total Packages	Total Weight	Total Declared Value†	Total Charges
1		\$ 1.00	
			Credit Card Auth.

†Our liability is limited to \$100 unless you declare a higher value. See back for details.

8 Release Signature

Sign to authorize delivery without obtaining signature.

By signing you authorize us to deliver this shipment without obtaining a signature and agree to indemnify and hold us harmless from any resulting claims.
Questions? Call 1-800-Go-FedEx (800-463-3339)
Visit our Web site at www.fedex.com
Rev. Date 11/98* Part #154815 ©1994-98 FedEx® PRINTED IN U.S.A. GBFE 2/00

360