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Title

CRADA Final Report: Mucin Mimic and Glycopeptide Synthesis

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CRADA Final Report
CRADA No. BG00-137(00)

1. Parties:

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2. Title of the Project: **Mucin Mimic and Glycopeptide Synthesis**

3. Summary of the specific research and project accomplishments:
(Were the goals of the CRADA achieved? Include relevant information but do not include proprietary or protected CRADA information.)

All specific aims of the proposal are accomplished as follows:

- (1) **Syntheses of aminoxy glycans such as GalNAc α -ONH₂ and Sia α 2,6GalNAc α -ONH₂ based on native mucin glycans.**
- (2) **Syntheses of homo- and copolymers functionalized with ketones for glycan attachment.**
- (3) **Ligations of glycans to polymers to generate artificial "glycodomains" of mucins.**

4. Deliverables:

Deliverable Achieved	Party (LBNL, Participant, Both)	Delivered to Other Party?
GalNAc α -ONH ₂	Ciba Vision	
Sia α 2,6GalNAc α -ONH ₂	Ciba Vision	
Ketone polymers	Ciba Vision	

5. Identify publications or presentations at conferences directly related to the CRADA?

- 1) Marcaurrelle, L. A.; Shin, Y.; Goon, S.; Bertozzi, C. R. "Synthesis of oxime-linked mucin mimics containing the tumor-related T(N) and sialyl T(N) antigens." *Org. Lett.* **2001**, *3*, 3691-3694.

6. List of Subject Inventions and software developed under the CRADA:
(Please provide identifying numbers or other information.)

None

7. A final abstract suitable for public release:

(Very brief description of the project and accomplishments without inclusion of any proprietary information or protected CRADA information.)

Mucus has several constituents but the most important are the mucins, heavily O-glycosylated proteins characterized by long stretches of tandem repeat sequences rich in glycosylated serine and threonine residues, with N- and C-terminal domains that have determined to a large extent by the viscous and viscoelastic properties of mucin glycoproteins. Indeed, these properties are evident in reconstituted purified mucin glycoproteins. Oligomeric mucin can be deconstructed into its monomeric components and then further into the domains that comprise each mucin molecule. There are two major domain types. "Glycodomains" are defined by stretches of the tandemly repeated Thr/Ser-rich segments that bear the characteristic O-linked glycans of the mucin molecule.

The goal of this project is to synthesize polymeric materials that mimic mucin glycodomains. In order to mimic the central features of mucin, these materials should have dense clusters of glycans that bear a similar structure to those found in native mucins, and a fairly rigid polymer backbone.

Four different polymers bearing ketone groups for the attachment of sugars were synthesized. GalNAc α -ONH₂ and Sia α 2,6GalNAc α -ONH₂ both of which could be ligated to the polymer scaffolds were synthesized. Mucin glycodomain mimics were successfully synthesized by ligation of glycans to polymers.

8. Benefits to DOE, LBNL, Participant and/or the U.S. economy.

The materials generated in this research will improve biomedical implants and the quality of life for those whose jobs demand the use of contact lenses. LBNL benefits by virtue of attracting top-notch scientists to the interface of biology and materials science. The US economy benefits by virtue of availability of new materials for commercial use.

9. Financial Contributions to the CRADA:

DOE Funding to LBNL	\$25,000
Participant Funding to LBNL	\$75,000
Participant In-Kind Contribution Value	\$0
Total of all Contributions	\$100,000

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