

Carbohydrate Microarrays for High-Throughput Analysis of Dendritic Cell-Glycan Interactions

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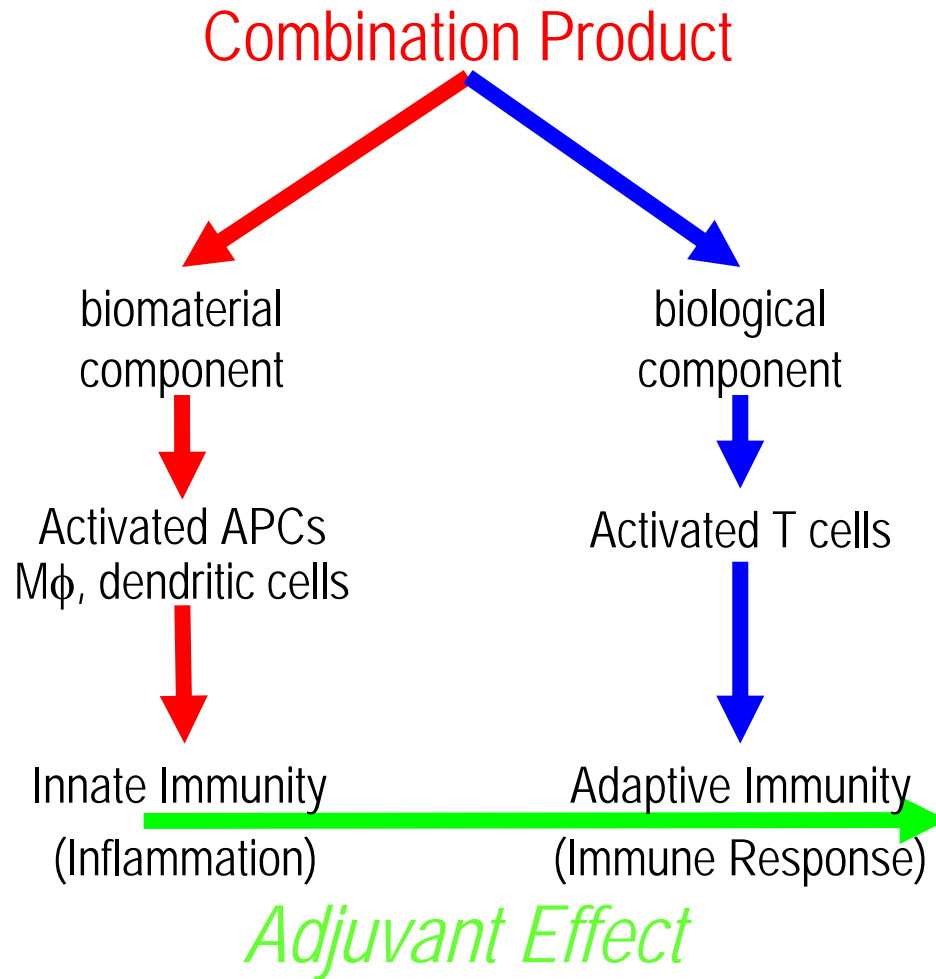
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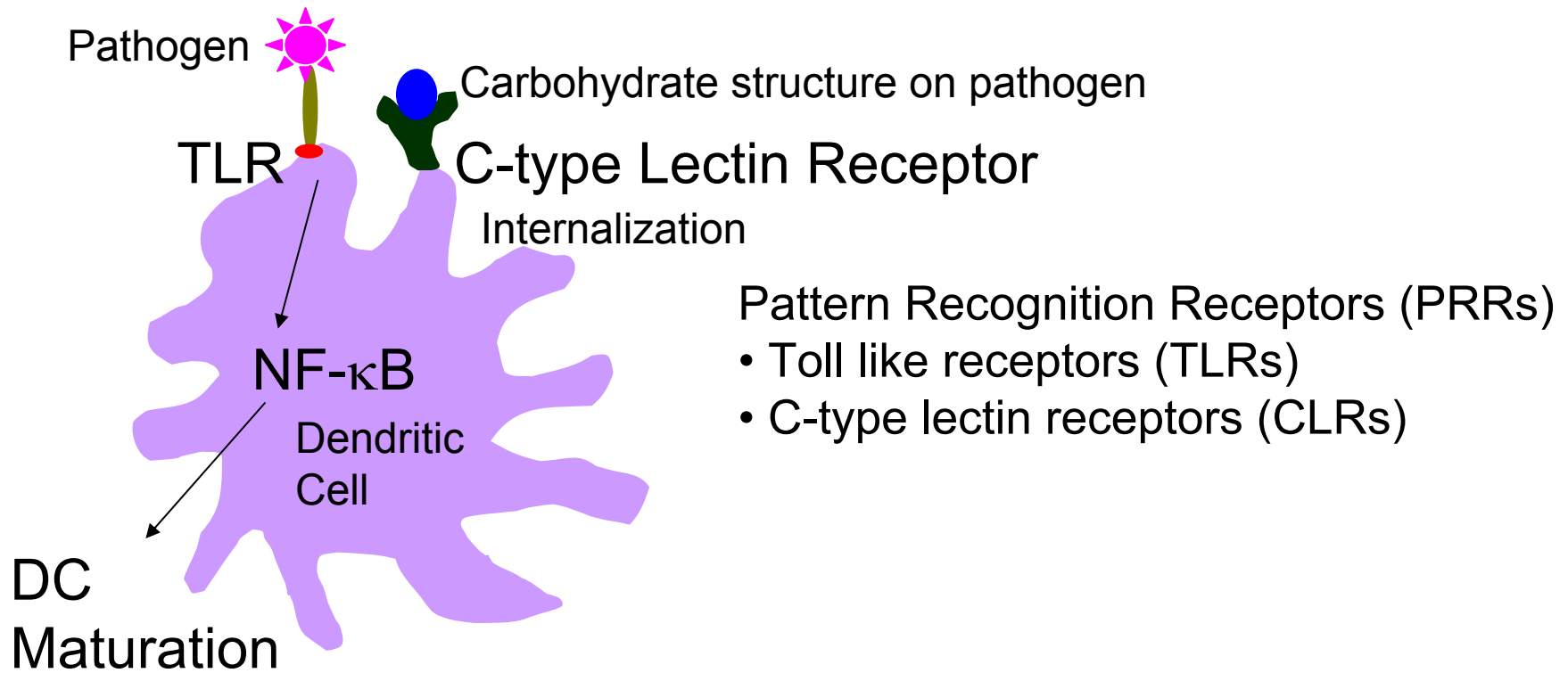


Complicated Host Response to a Combination Product





DC Pathogen Recognition Process

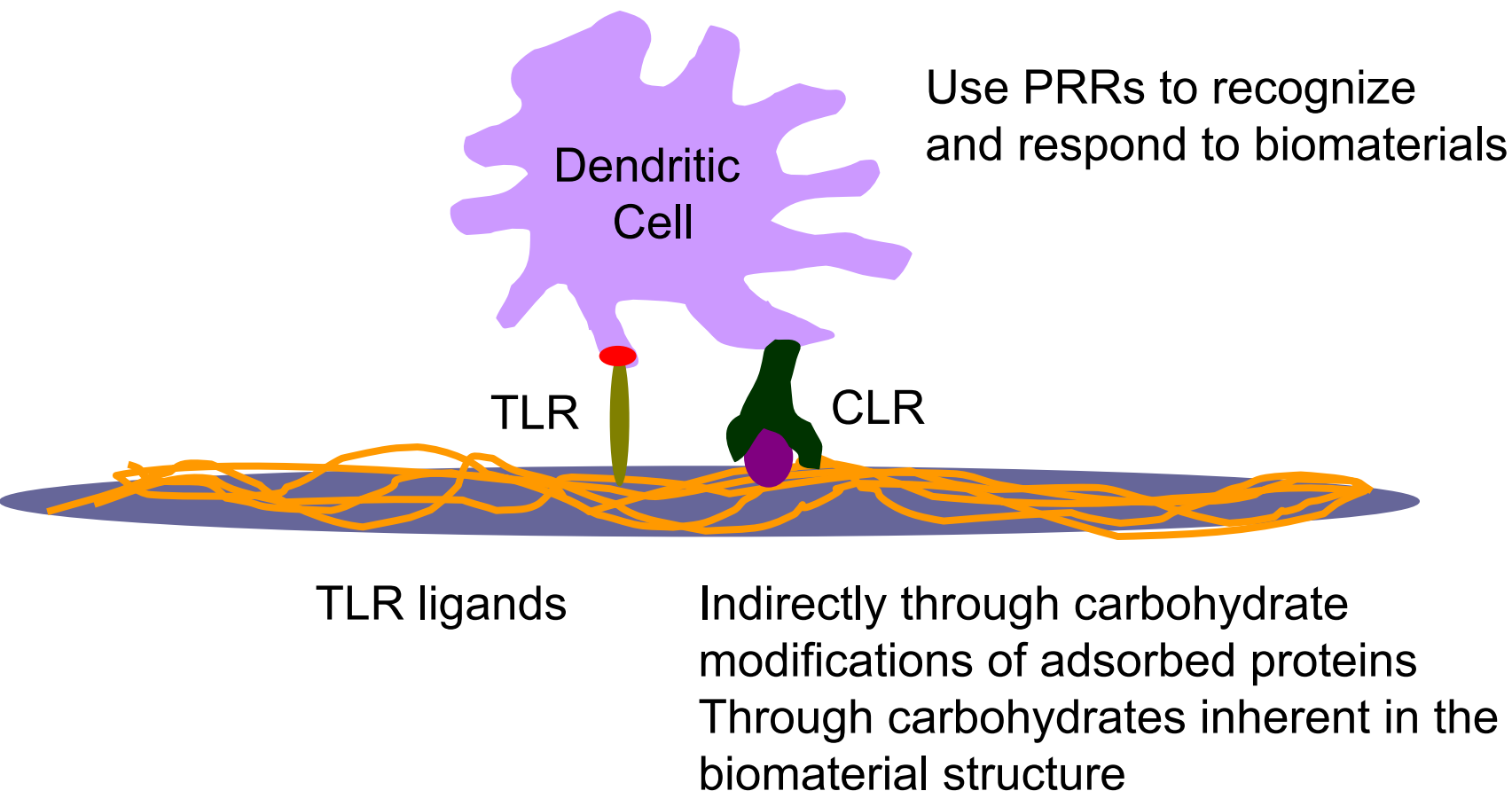


- Pattern Recognition Receptors (PRRs)
- Toll like receptors (TLRs)
 - C-type lectin receptors (CLRs)

- Pathogen Associated Molecular Patterns (PAMP)
- E.g., TLR-4 recognizes LPS
 - E.g., Macrophage mannose receptor recognizes mannose, fucose, sLe(x), N-acetylglucosamine

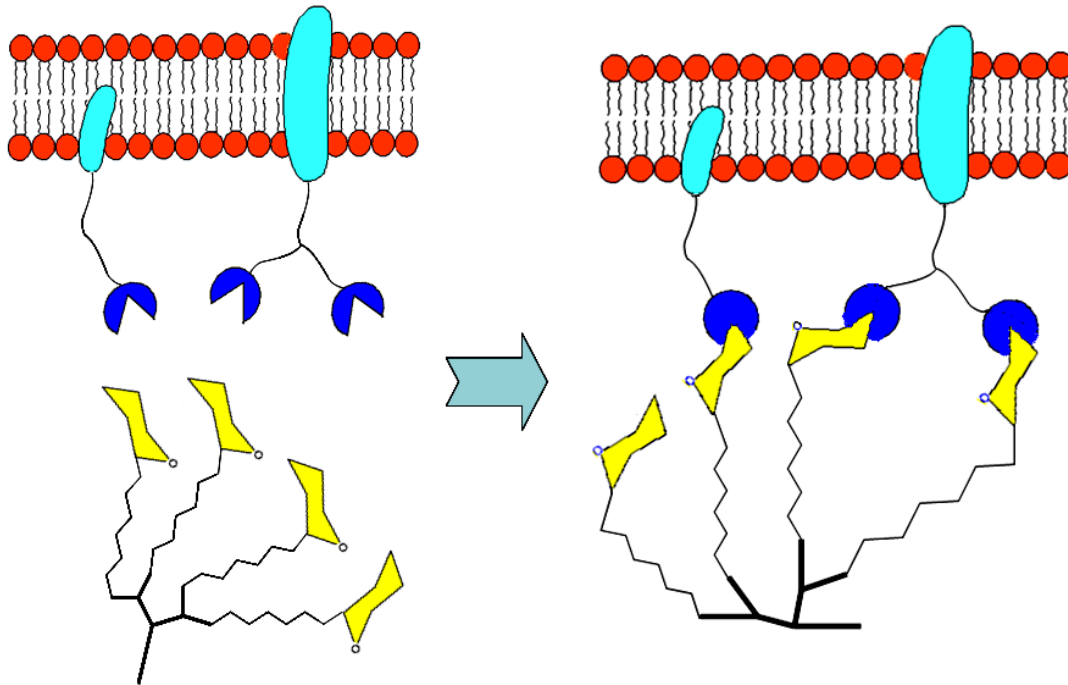


DC Recognition of and Response to Biomaterial





Dynamics of Glycan-GBP Interactions



Micro/nano domain compatibility

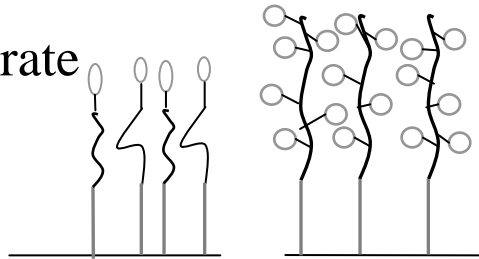
Multivalency

-Glycans and glyco-binding receptors typically have weak affinity (K_d of micromolar to millimolar).

Multivalent mechanisms are usually involved, which can lead to enhanced interactions and recognition between carbohydrate ligands and cells.

Bioengineering of Functional Glycans

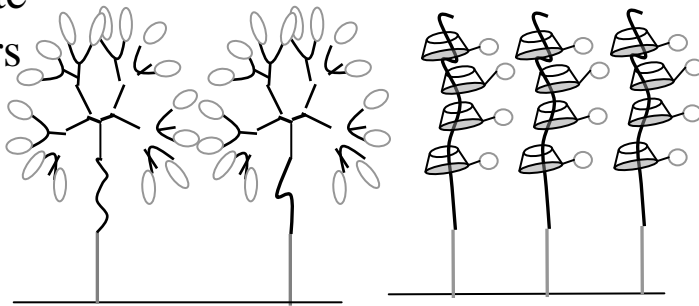
Carbohydrate ligand



Carbohydrate brushes

What are molecular and nano features of glycan ligands?

Carbohydrate nano-clusters



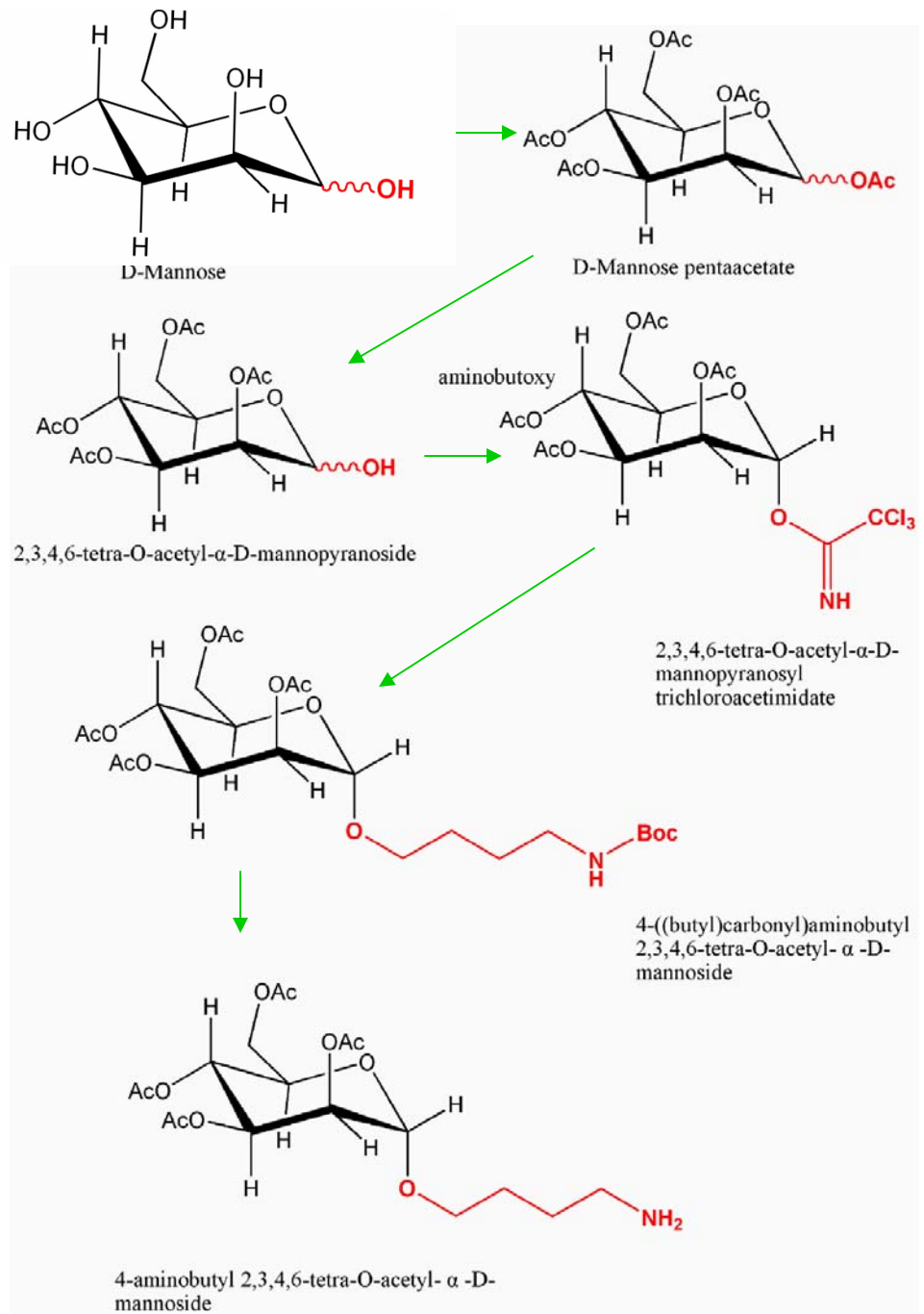
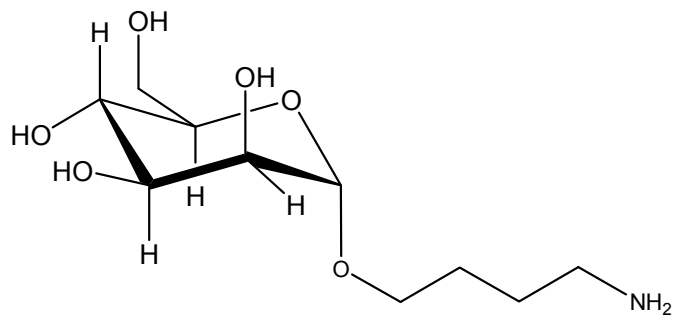
Carbohydrate rotaxanes

Whether we could identify them in a high throughput manner?

Designing carbohydrate conjugates for architectural control of ligand presentation.

Our Aims

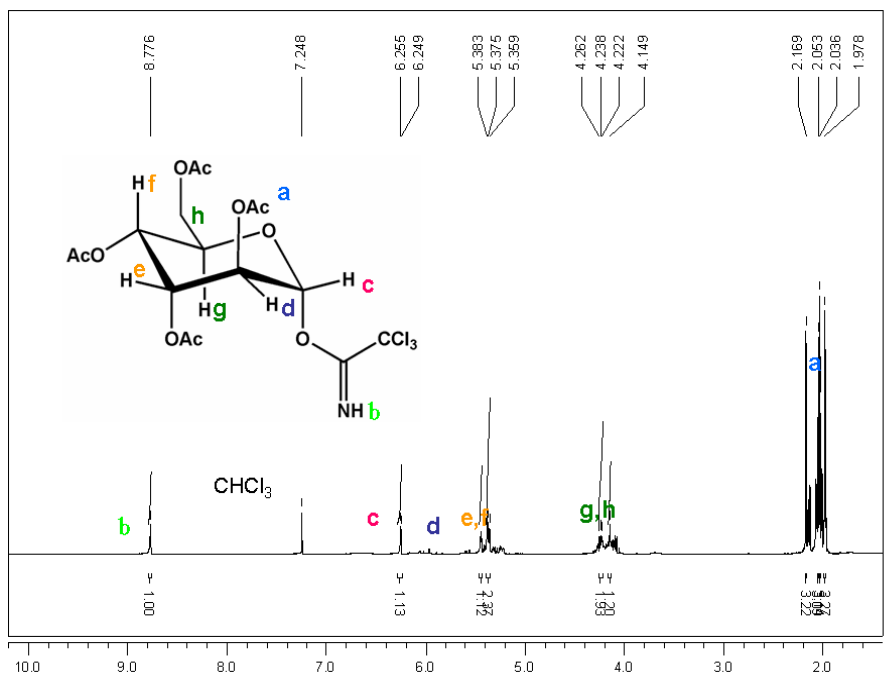
- **Specific Aim # 1: To synthesize multivalent carbohydrate ligands**
- **Specific Aim # 2: Examine DC responses to carbohydrate microarrays with varied carbohydrate presentation**



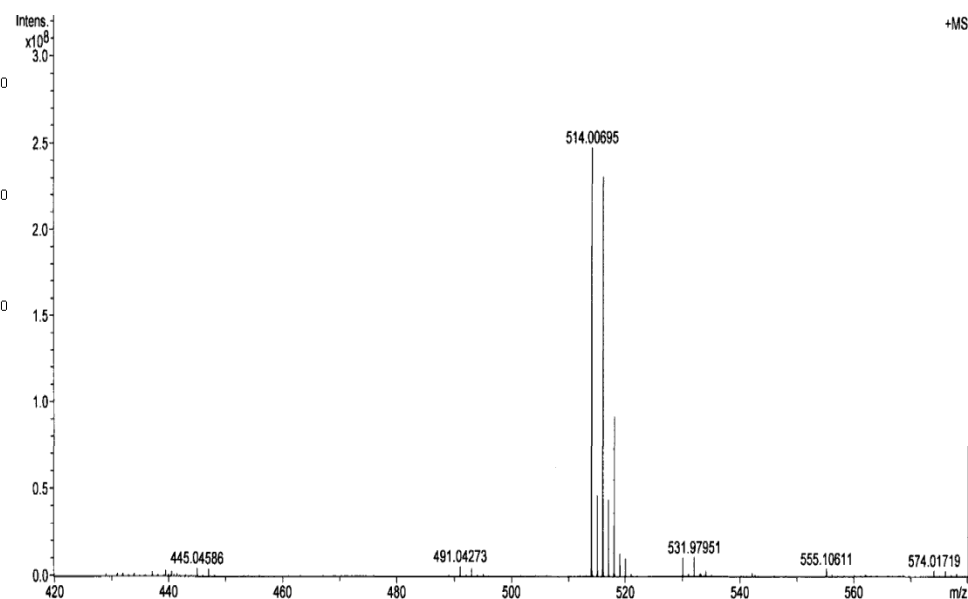
■ Ying's New Lab

■ Student:
Xiaopeng Liu

2,3,4,6-tetra-O-acetyl- α -D-mannopyranosyl trichloroacetimidate

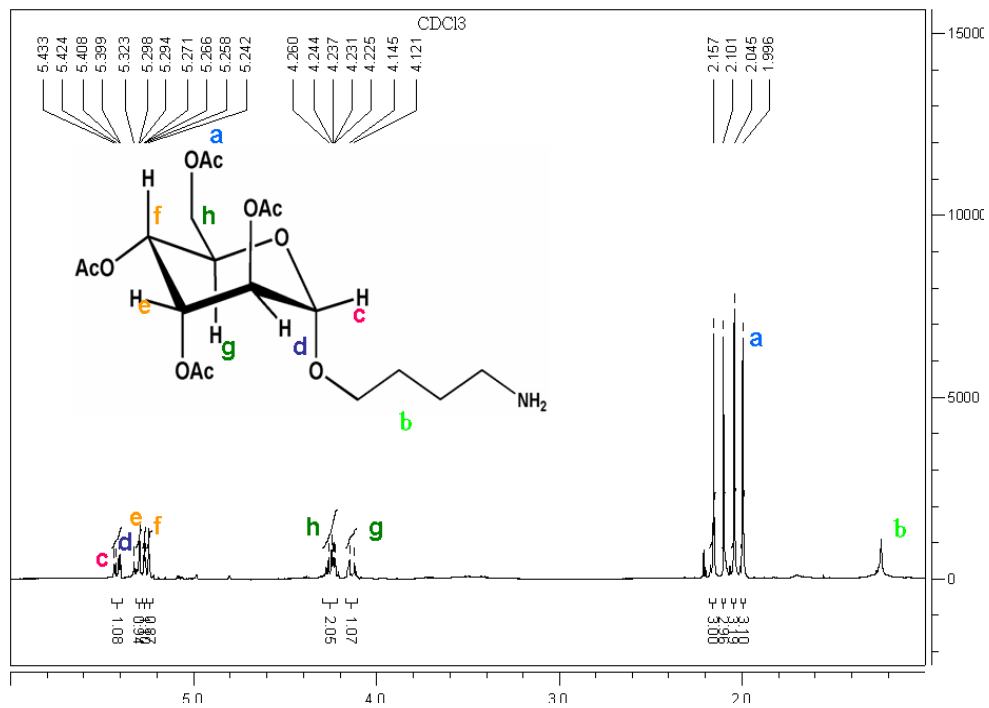


NMR

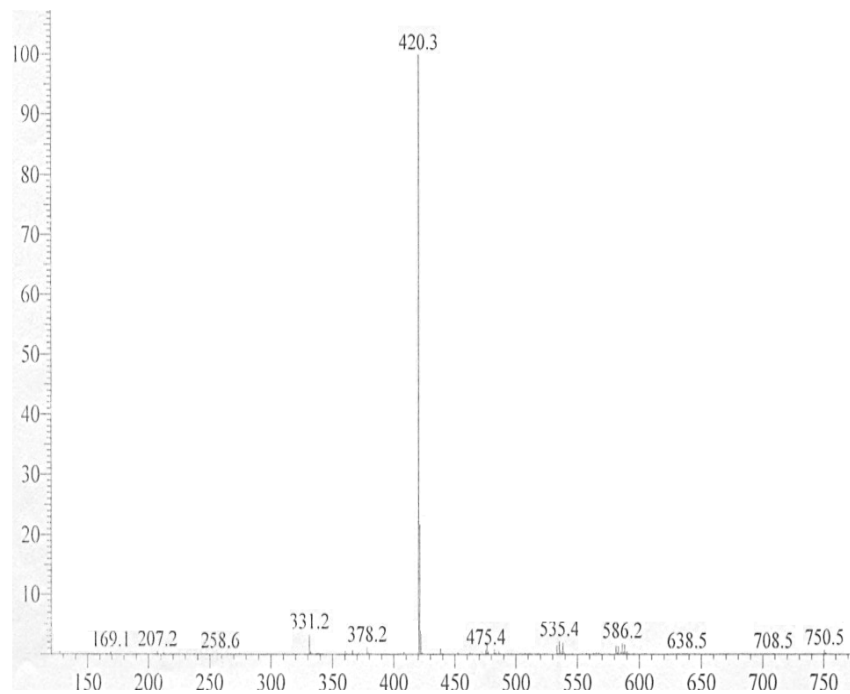


MS

4-aminobutyl 2,3,4,6-tetra-O-acetyl- α -D-mannoside

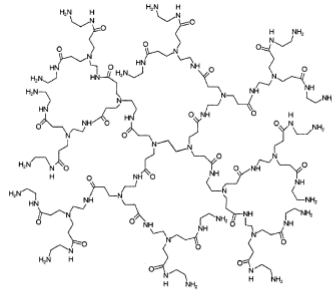


NMR

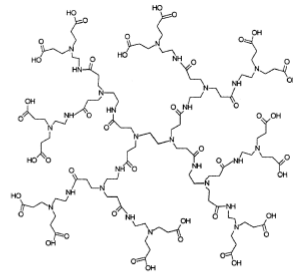


MS

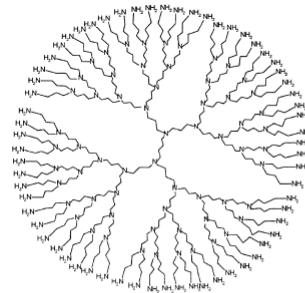
Dendrimers and Poly (amidoamine) (PAMAM)



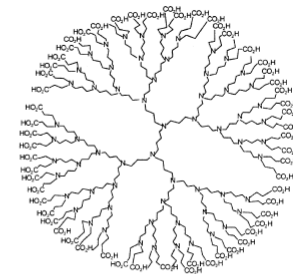
PAMAM
(Amine terminated)



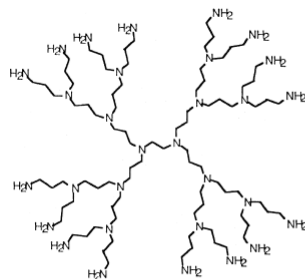
PAMAM
(Carboxylic acid terminated)



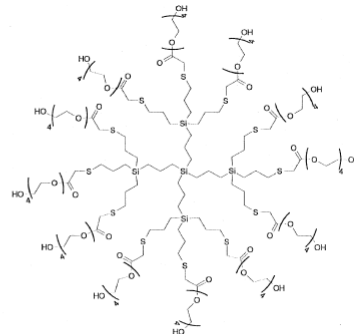
DAB-dendrimers
(Amine terminated)



DAB-dendrimers
(Carboxylic acid terminated)



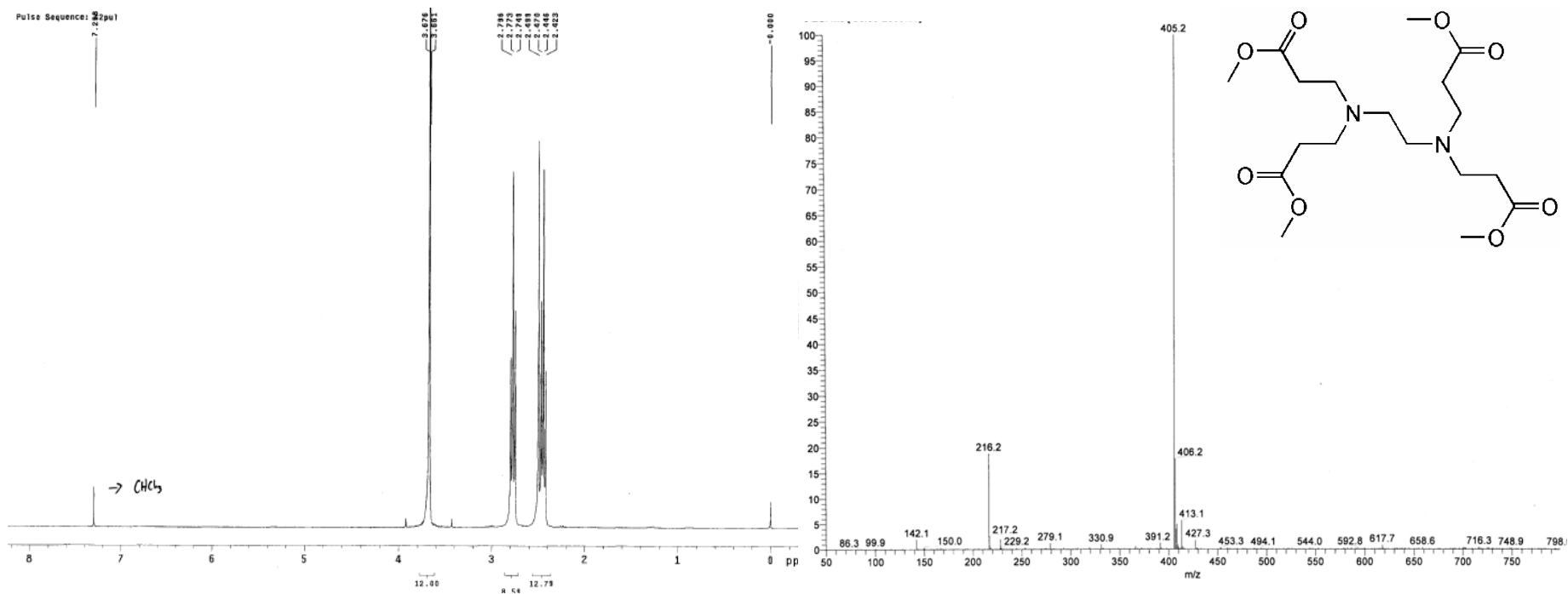
DAE-dendrimers
(Amine terminated)



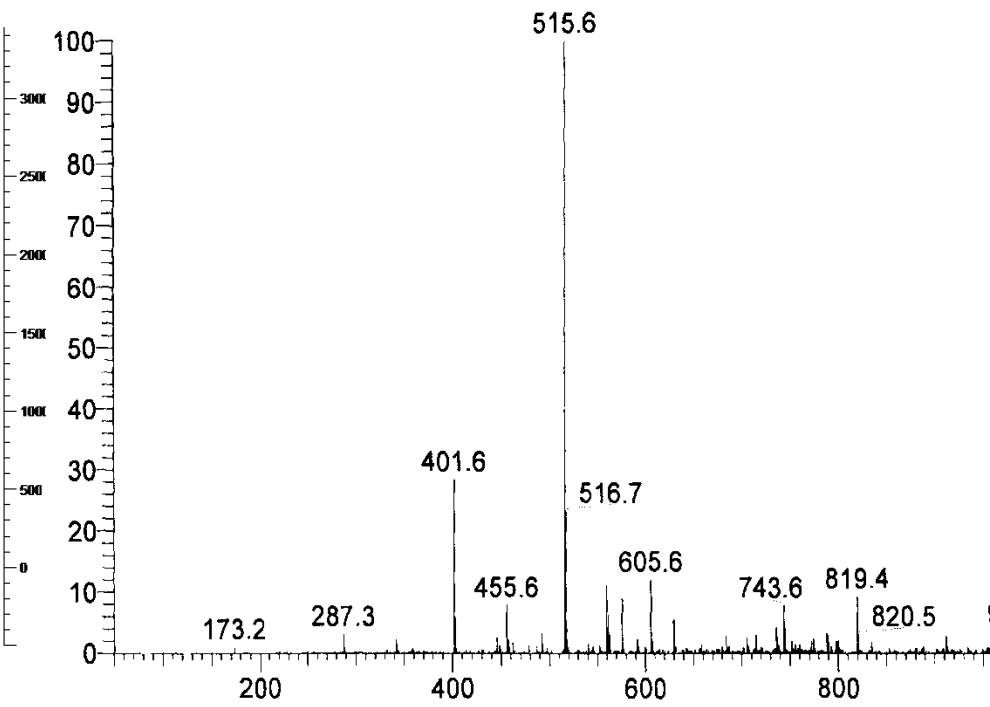
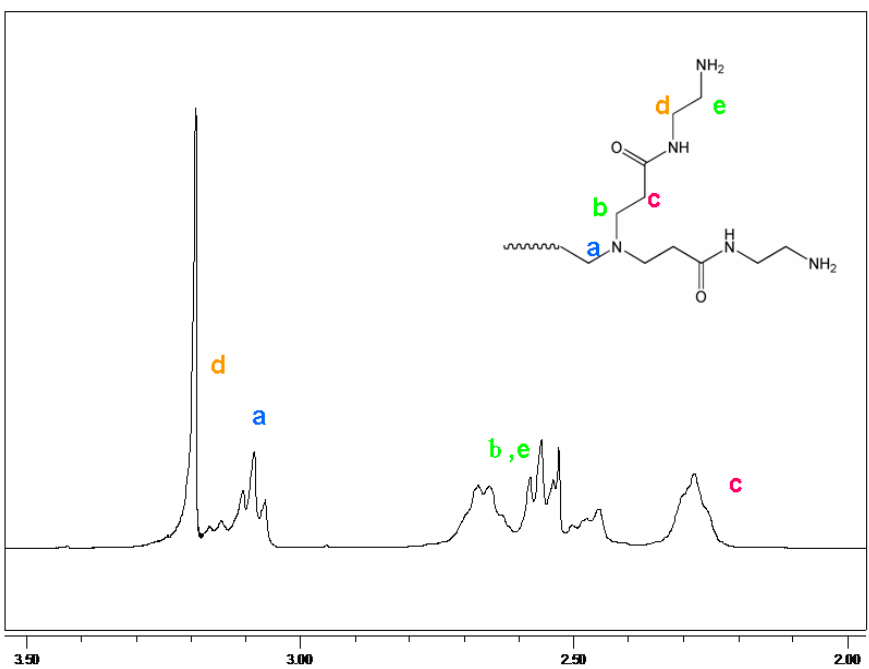
CSi-PEO dendrimers

Hyperbranched
structures suitable
for controlling
surface composition
and organization

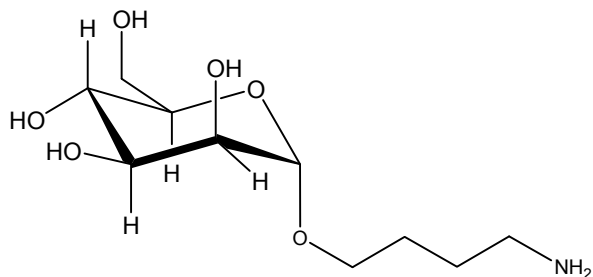
PAMAM G0.5



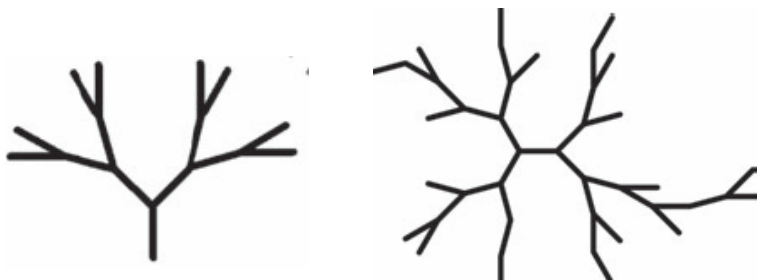
PAMAM G1



What's NEXT?

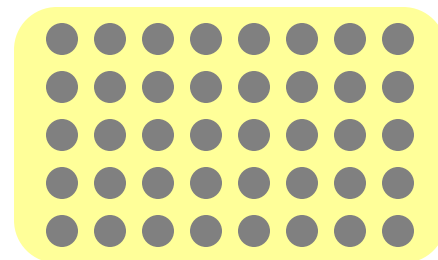


**Mannose
N-acetylglucosamine**



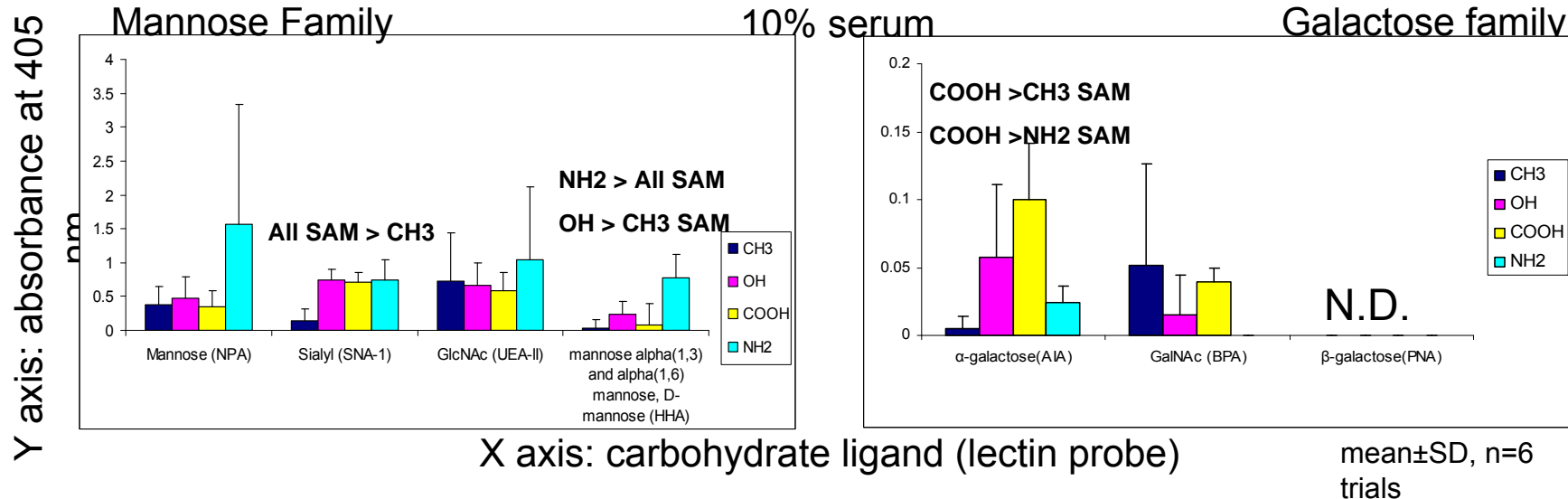
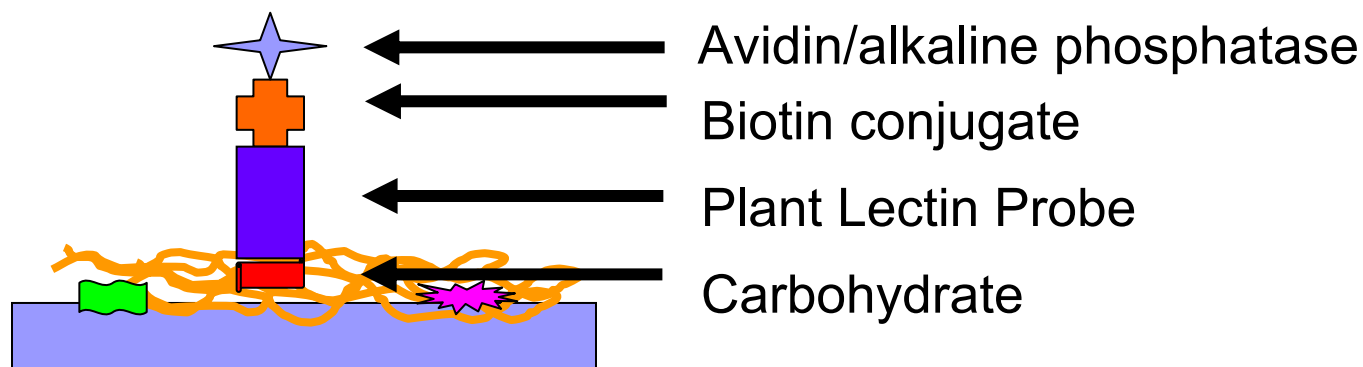
**Structurally
correlated
synthetic
libraries**

A combinatorial approach



Conjugation and Arraying

Differential carbohydrate profiles on different biomaterials

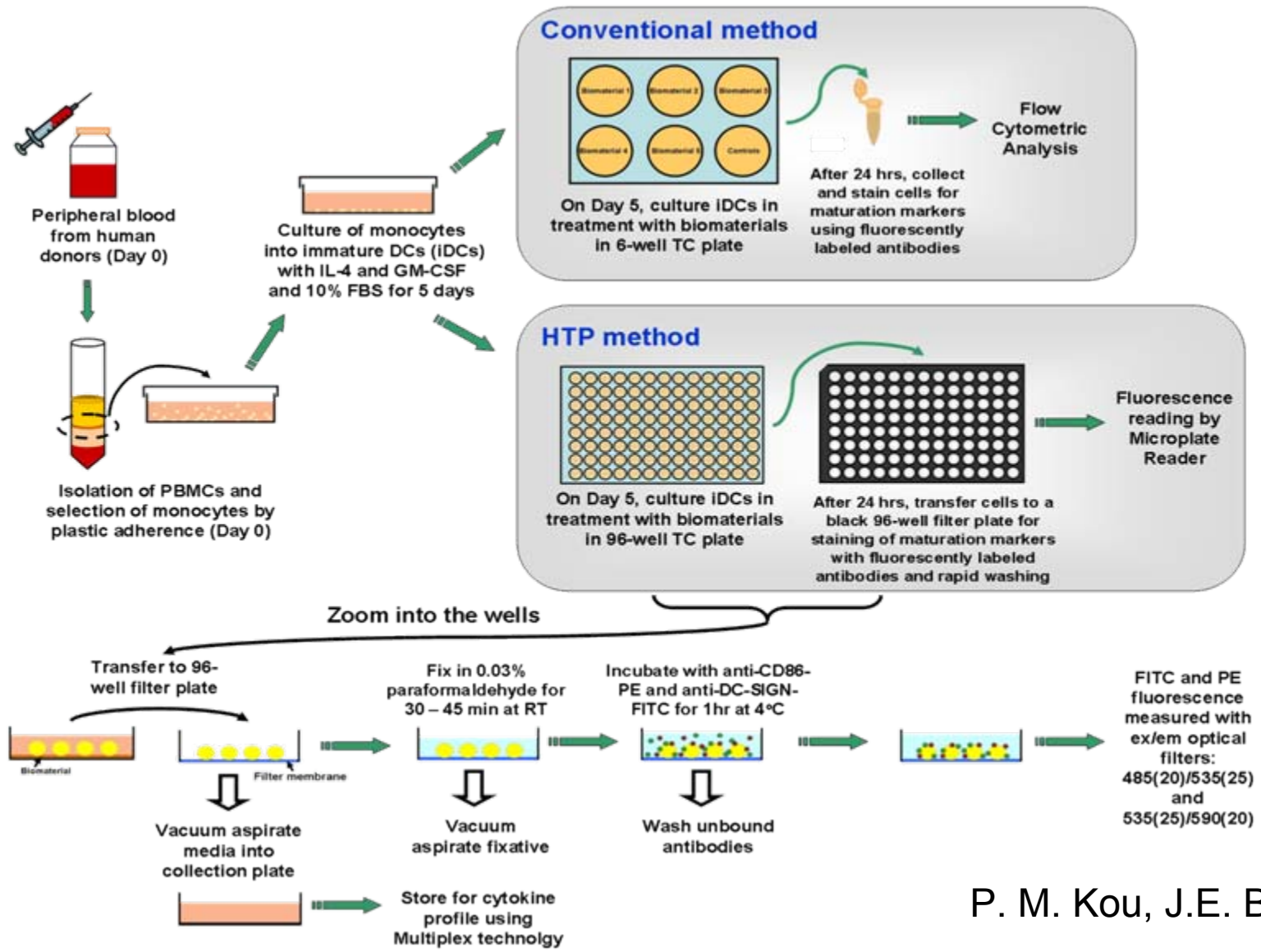


Role of Glycans in DC Recognition of and Responses to Biomaterials

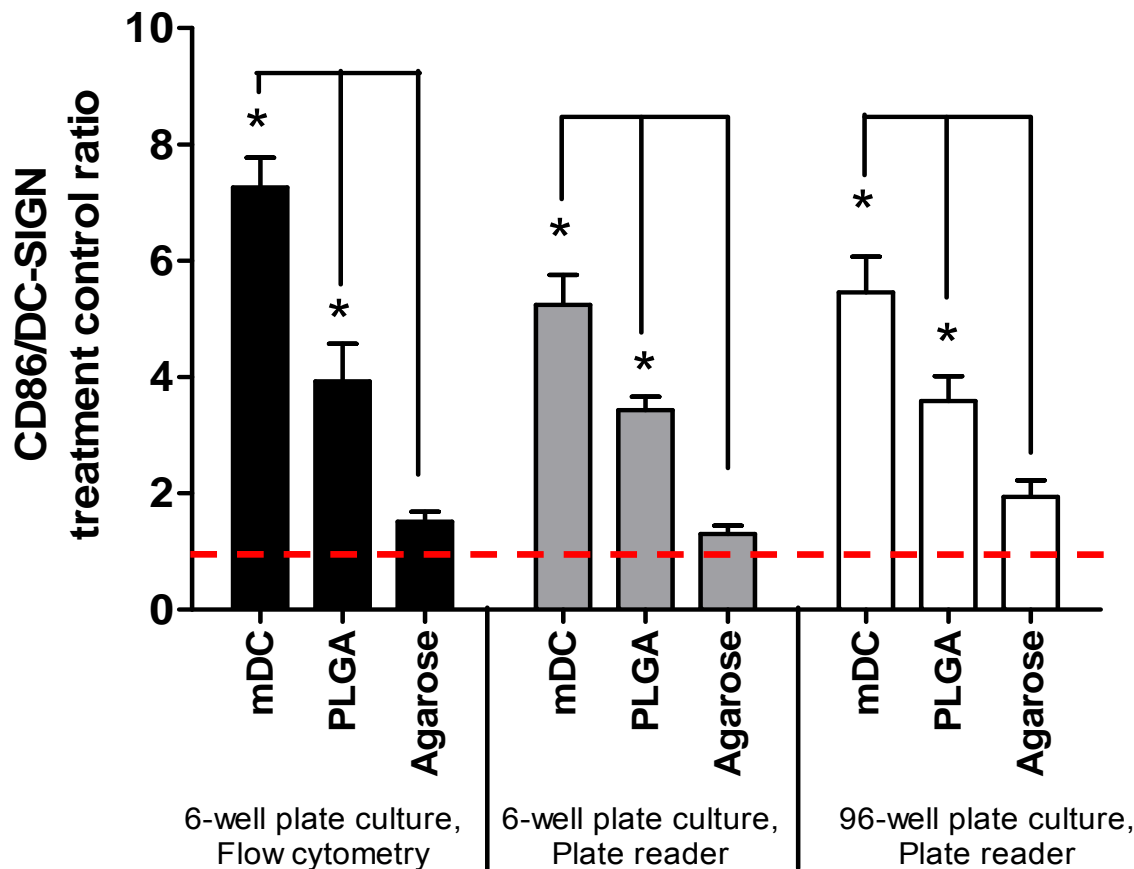
S. Shankar, I.I. Chen, J.E. Babensee



Conventional and High Throughput Methodology for Assessment of DC Responses to Biomaterials



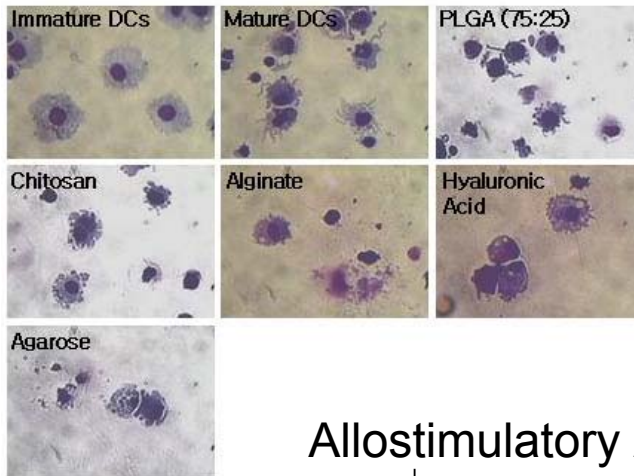
Validation of The HTP Methodology



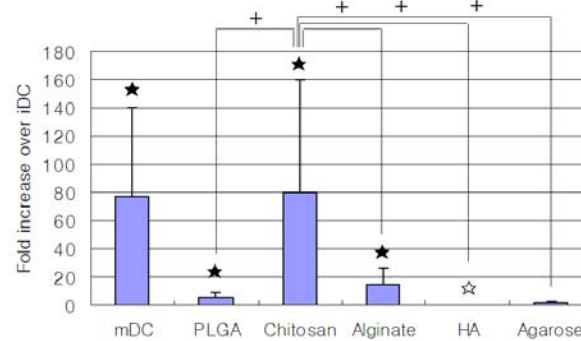
Biomaterial study with PLGA and agarose. Comparison of treatment to control (iDCs) ratios of CD86/DC-SIGN for DCs treated with biomaterials in 6-well format by FC (black bars), 6-well format by fluorescence plate read (grey bars), and 96-well format by fluorescence plate read (white bars), as compared to immature DCs. * or Brackets: $p < 0.05$ P. M. Kou, J.E. Babensee

Array of Immunological Assays to Study DC Responses to Biomaterials

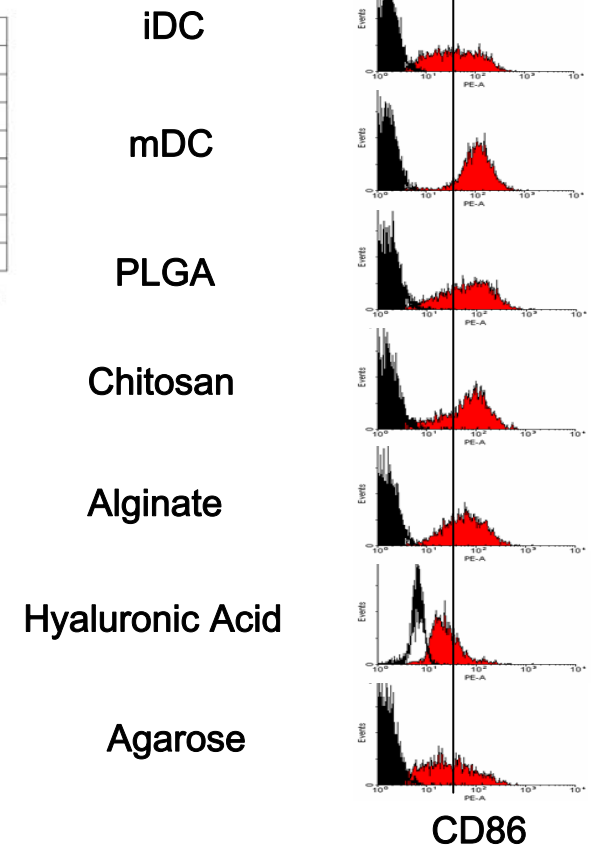
Cell Morphology



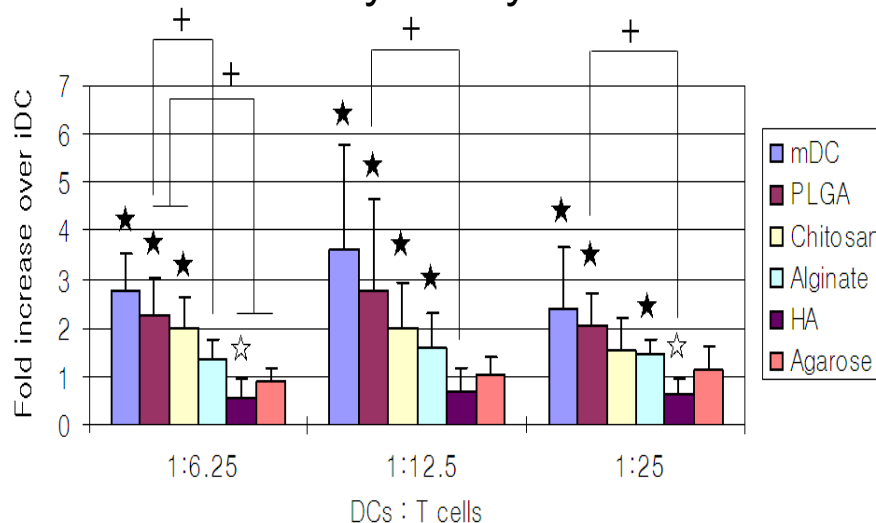
ELISA for Cytokine Release - TNF α



Flow Cytometry

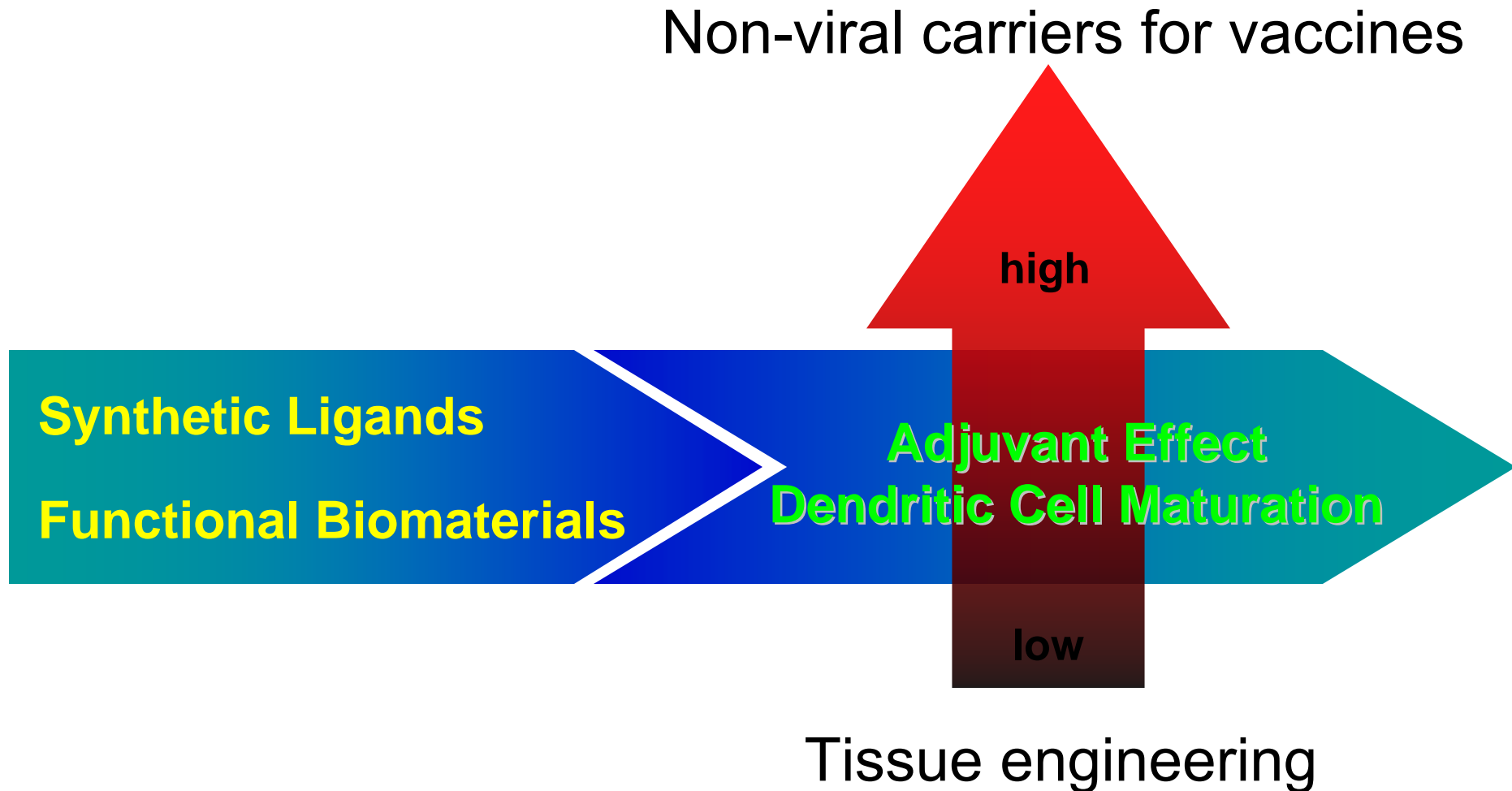


Allostimulatory Ability in an MLR





Engineering and Applications



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