Dendritic Cell Responses to a Library of Polymethacrylates with Varied Material Properties

Peng Meng Kou*, Narayanan Pallassana‡, Barry Cunningham‡, Joachim Kohn‡, and Julia E. Babensee*
*Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA 30332; ‡Department of Chemistry and Chemical Biology, Rutgers University, and New Jersey Center for Biomaterials, Piscataway, NJ 08854

Statement of Purpose: Biomaterials are widely used as the carriers of biologics in combination products for tissue regeneration or vaccine delivery. The host immune response to the immunogenic biological components may be modulated by the biomaterial components. Dendritic cells (DCs), the most potent antigen presenting cells, are critical in bridging innate to adaptive immunity. Controlling the phenotype of DCs through the biomaterial component is a novel immunomodulation strategy.

A differential biomaterial effect has been observed on the resultant DC phenotype. For example, functional DC maturation was induced by poly(lactic-*co*-glycolic acid) (PLGA) or chitosan films, not induced by agarose or alginate films, and inhibited by hyaluronic acid films[1,2]. However, it was unclear which material properties contributed to such differential effects. A 96-well filter plate-based high throughput (HTP) method was developed to allow for the screening of DC phenotype upon treatment with biomaterial surfaces with graded variations in properties. This HTP methodology was used to analyze the effects of a library of polymethacrylates (pMAs) on DC phenotype. The material properties of pMAs, including contact angle, glass transition temperature (T_g), surface roughness, and surface chemical composition, were characterized and compared to the trend of DC phenotype upon treatment with the pMAs. Understanding the correlations between material properties and DC phenotype will provide insights into how biomaterials affect functional immune responses through their immunomodulatory effects on DCs.

Methods: Twelve different pMAs of varying material properties were selected for analysis as to resultant DC responses upon treatment. pMA-coated wells were prepared by a novel solvent casting procedure into wells of a 96-well polypropylene (PP) plate. For sterilization, pMA-coated plates were exposed to UV (30 min). DC cytotoxicity upon treatment with pMAs was measured by their release of glucose-6-phosphate dehydrogenase (G6PD) (Vybrant Cytotoxicity Assay, Molecular Probes).

DCs, derived from human peripheral blood mononuclear cells[2], were treated with pMAs for 24 hours in 96-well plates. DC maturation was compared to controls: untreated immature DCs (iDCs) and lipopolysaccharide-treated mature DCs (mDC) cultured on TCPS 96-well plate in parallel. All treated DCs and controls were transferred to a black 96-well filter plate and the ratio of CD86/DC-SIGN, a cell number-independent maturation metric, was analyzed by immunostaining. The supernatants were collected into a 96-well plate and a portion processed immediately for G6PD release for cytotoxicity testing or stored at -80°C for multiplex cytokine profiling.

Results/Discussions: This collaborative work is the first feasibility demonstration of a new HTP testbed that can be used to explore a wide range of cell-material interactions. Here, the trend of biomaterial-induced DC maturation was explored. The trend represented by the metric CD86/DC-SIGN ratio was similar to the trend of pro-inflammatory cytokines (e.g. TNF-α) and chemokines (e.g. IL-8), while the trend of DC maturation inverse to the trend of anti-inflammatory cytokine production (e.g. IL-16) (Fig. 1). These trends of DC phenotype paralleled the trend of contact angle of the pMAs. None of the biomaterials induced cytotoxicity different from iDC control. Because the endotoxin content of all the coated pMAs were below 0.1 EU/ml, the observed biological response was resultant from biomaterial treatment.

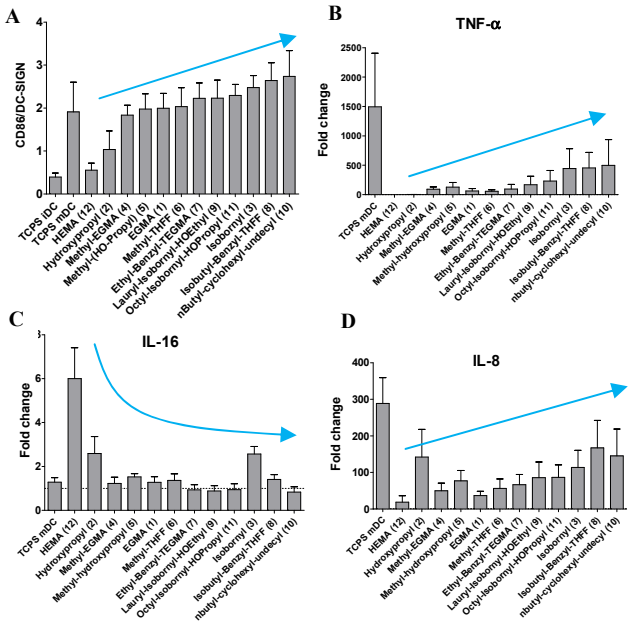

Figure 1: DC responses, CD86/DC-SIGN expression (A), TNF-α (B), IL-16 (C) and IL-8 (D) release, to a library of pMAs, mean ± SEM, n=6 donors, 11 plates.

Conclusions: The trends of DC phenotype were similar to the trend of material properties of pMAs, such as water contact angle. The correlations between material properties and DC phenotype will be further analyzed and can provide guidelines for future biomaterial design. This HTP pMA testbed can also be used to study the biomaterial-induced response of other cell types.

Acknowledgements: Financial support from an NSF CAREER grant (BES-0239152) and NIH grant 1RO1 EB004633-01A1. The 96-well pMA testbed was developed under NIH grant EB001046 (RESBIO) at NJ Center for Biomaterials, Rutgers University.

References: 1. Babensee JE, Paranjpe A, J Biomed Mater Res, 2005, 74A: 503-510. 2. Yoshida M, Babansee JE, J Biomed Mater Res, 2004, 71A: 45-54.