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ORIGINAL ARTICLE

Activation of Polymorphonuclear Leukocytes by Candidate Biomaterials for an Implantable Glucose Sensor

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Abstract

Background:

Continuous monitoring of glucose by implantable microfabricated devices offers key advantages over current transcutaneous glucose sensors that limit usability due to their obtrusive nature and risk of infection. A successful sensory implant should be biocompatible and retain long-lasting function. Polymorphonuclear leukocytes (PMN) play a key role in the inflammatory system by releasing enzymes, cytokines, and reactive oxygen species, typically as a response to complement activation. The aim of this study was to perform an *in vitro* analysis of PMN activation as a marker for biocompatibility of materials and to evaluate the role of complement in the activation of PMN.

Methods:

Fifteen candidate materials of an implantable glucose sensor were incubated in lepirudin-anticoagulated whole blood. The cluster of differentiation molecule 11b (CD11b) expression on PMN was analyzed with flow cytometry and the myeloperoxidase (MPO) concentration in plasma was analyzed with enzyme-linked immunosorbent assay. Complement activation was prevented by the C3 inhibitor compstatin or the C5 inhibitor eculizumab.

Results:

Three of the biomaterials (cellulose ester, polyamide reverse osmosis membrane, and polyamide thin film membrane), all belonging to the membrane group, induced a substantial and significant increase in CD11b expression and MPO release. The changes were virtually identical for these two markers. Inhibition of complement with compstatin or eculizumab reduced the CD11b expression and MPO release dose dependently and in most cases back to baseline. The other 12 materials did not induce significant PMN activation.

Conclusion:

Three of the 15 candidate materials triggered PMN activation in a complement-dependent manner and should therefore be avoided for implementation in implantable microsensors.

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Abbreviations: (A2020) araldite 2020, (AAO) aluminium oxide, (ANOVA) analysis of variance, (CD11b) cluster of differentiation molecule 11b, (CM) cellulose ester, (CT) ceramTec GC, (ConA) concanavalin A, (DP) DuPont 951, (ETek) epo-Tek 353ND, (ISF) interstitial fluid, (LTCC) low-temperature cofired ceramic, (Me) stainless steel, (MFI) mean fluorescence intensity, (MPO) myeloperoxidase, (MWCO) molecular weight cut off, (PAR) polyamide reverse osmosis membrane, (PATF) polyamide thin film membrane, (PBS) phosphate buffer saline, (PC) polycarbonate, (PDMS) polydimethylsiloxane, (PMN) polymorphonuclear leukocyte, (ROI) reactive oxygen intermediate, (S3140) silicone 3140, (S3145) silicone 3145, (Si) silicon, (SiO_2) silicon dioxide

Keywords: biocompatibility, biomaterials, complement, implantable device, polymorphonuclear leukocyte

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