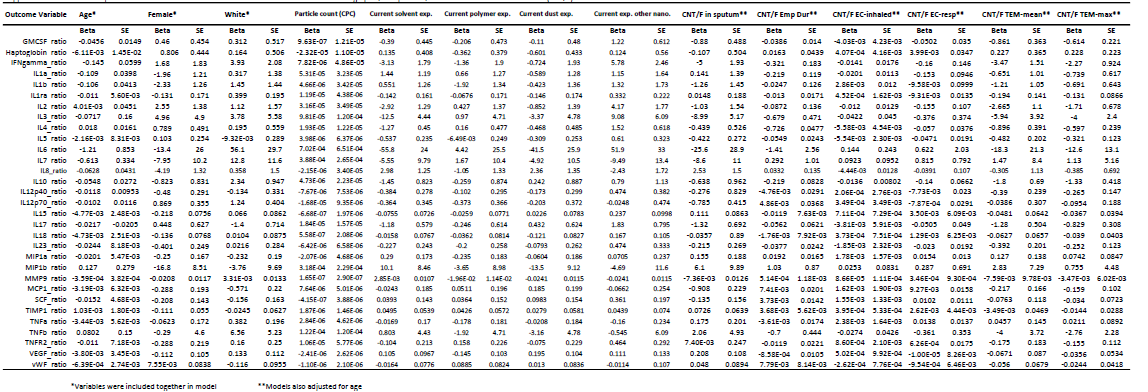
Supplemental Table 1. Description of biomarkers used in TruCulture assay. Bold indicates biomarker showed sufficient response after stimulation to include in modeling analysis.

|  |  |  |
| --- | --- | --- |
| **Biomarker name** | **Abbreviation** | **Biomarker description** |
| Alpha-1-antitrypsin | AAT | Liver protein that blocks the destructive effects of certain enzymes |
| Alpha-2-macroglobulin | A2Macro | Major plasma protein; functions include ion transport, carrier protein, and proteinase inhibition |
| Beta-2-microglobulin | B2M | Protein found on surface of all nucleated cells, shed into blood particularly by tumor cells and lymphocytes |
| Brain-derived neurotrophic factor | BDNF | Protein found in neurons, helping support their survival & genesis |
| C-reactive protein | CRP | Acute phase protein related to inflammatory diseases, infections, and neoplastic diseases |
| Complement C3 | C3 | Immune system protein involved in activating complement system |
| Eotaxin-1 | Eotaxin | Protein produced by epithelial & endothelial cells and eosinophils, whose expression is enhanced in allergic inflammation |
| Factor VII | FactorVII | Protein involved in blood coagulation cascade |
| Ferratin | FRTN | Protein reflecting iron stores in body or elevated in inflammation |
| Fibrinogen | Fibrinogen | Plasma glycoprotein involved in coagulation; high levels associated with cardiovascular disease (CVD) and stroke. |
| **Granulocyte-macrophage colony-stimulating factor** | GM\_CSF | Cytokine that controls granulocytes & macrophages in hematopoiesis |
| **Haptoglobin** | Haptoglobin | Acute phase protein that binds free hemoglobin in blood |
| Intercellular adhesion molecule 1 | ICAM1 | Cell surface receptor involved in inflammation, CVD, & diabetes |
| **Interferon gamma** | IFNγ | Cytokine involved in delayed type hypersensitivity & inflammation |
| **Interleukin-1 alpha** | IL1α | Immuno-modulator that mediates a wide range of inflammatory responses |
| **Interleukin-1 beta** | IL1β | Immuno-modulator that mediates a wide range of inflammatory responses |
| **Interleukin-1 receptor agonist** | IL1ra | Protein that acts as an IL-1 inhibitor; balance plays role in inflammation |
| **Interleukin-2** | IL2 | Central regulator of immune response; role in anti-inflammatory reactions |
| **Interleukin-3** | IL3 | Protein produced by T-cells following activation by antigens or leukocytes |
| **Interleukin-4** | IL4 | Produced by T-cells and most biologically active helper cells for B-cells |
| **Interleukin-5** | IL5 | Growth factor responsible for growth & differentiation of eosinophils |
| **Interleukin-6** | IL6 | Cytokine released in response to stimuli & in inflammation or infection |
| **Interleukin-7** | IL7 | Stimulates proliferation of B cells; supports megakaryocyte maturation |
| **Interleukin-8** | IL8 | Chemokine produced by macrophages that attracts other leukocytes |
| **Interleukin-10** | IL10 | Produced by Th1 & Th2 cells; antagonist of IFNγ |
| **Interleukin-12 subunit p40** | IL12p40 | Produced by B-cells in response to bacteria & parasites; also show tumor-inhibitory properties |
| **Interleukin-12 subunit p70** | IL12p70 |
| **Interleukin-15** | IL15 | Stimulates T-cell proliferation; similar to IL2 |
| **Interleukin-17** | IL17 | Recruits monocytes & neutrophils to inflammation sites |
| **Interleukin-18** | IL18 | Pro-inflammatory cytokine produced by macrophages & other leukocytes |
| **Interleukin-23** | IL23 | Produced by dendritic cells & macrophages; important in inflammation |
| **Macrophage inflammatory protein-1 alpha** | MIP1α | Produced by macrophages in response to bacterial endotoxins; involved in activation of granulocytes; induce synthesis of cytokines IL1, IL6 & TNF |
| **Macrophage inflammatory protein-1 beta** | MIP1β |
| Matrix metalloproteinase-3 | MMP3 | Degrades extracellular matrix substrates & inactivates proteinase inhibitors |
| **Matrix metalloproteinase-9** | MMP9 | Degrades proteins in extracellular matrix & activates growth factors |
| **Monocyte chemotactic protein 1** | MCP1 | Helps recruit monocytes to sites of injury & infection |
| **Stem cell factor** | SCF | Induces differentiation in lymphoid & erythroid progenitor cells & mast cells |
| T-cell-specific protein RANTES | RANTES | Chemotactic protein for T-cells & granulocytes; recruits leukocytes |
| **Tissue inhibitor of metalloproteinases 1** | TIMP1 | Involved in biosynthesis of connective tissue; complexes with MMPs |
| **Tumor necrosis factor alpha** | TNFα | Secreted by macrophages; can induce cell death of some tumor cell lines |
| **Tumor necrosis factor beta** | TNFβ | Produced by T-lymphocytes, cytotoxic for a wide range of tumor cells |
| **Tumor necrosis factor receptor 2** | TNFR2 | Neutralizes the biological activity of TNFα and TNFβ |
| Vascular cell adhesion molecule-1 | VCAM1 | Supports adhesion of leukocytes; has role in inflammatory immune response |
| **Vascular endothelial growth factor** | VEGF | Induces endothelial cells; inhibits apoptosis; induces permeability of vessels |
| Vitamin D-binding protein | VDBP | Protein in plasma & other tissues that carries vitamin D sterols |
| **von Willebrand factor** | vWF | Acute phase reactant; promotes adhesion of platelets to vascular injury sites |

\*Description source: <https://myriadrbm.com/products-services/humanmap-services/humanmap/>

Supplemental Table 2. Model parameter estimates for Box-Cox transformed biomarker ratios with demographic, occupational, and carbon nanotube or nanofiber (CNT/F) metrics



Supplemental Fig. 1. Most significant canonical pathway of effects related to TEM-max. The pathway, role of cytokines in mediating communication between immune cells, illustrates a general suppression of cytokine production (green color indicates reduced levels with increasing TEM-max) of circulating leukocytes following a secondary challenge. Of note, the effects appear to be generalized and not related to any specific cell population.

