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Vaccine hyporesponse in healthy elderly subjects is associated with a decrease in B cell IFNα responses: Data from functional proteomic analysis using single cell network profiling

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Abstract

Predicting vaccine efficacy has challenged developers for decades. Single cell network profiling (SCNP) is a multiparametric flow cytometry-based approach that simultaneously measures evoked intracellular signaling in multiple and highly specific cell subsets. SCNP technology was used to identify biology associated with vaccine hyporesponse in elderly healthy subjects. Cryopreserved pre-vaccination peripheral blood samples from 174 healthy [144 elderly (≥65 years) and 30 young (24-40 years)] subjects vaccinated with Tetanus, Diphtheria, Hepatitis A, Hepatitis B, and Cholera were examined. Vaccine hyporesponse was defined as non-response to both Hepatitis B and Cholera based on post-vaccination antibody titers. Twenty-six signaling nodes (extracellular modulator→intracellular readout) were analyzed within 7 distinct immune cell subsets in peripheral blood mononuclear cells. The Wilcoxon rank-sum test was used to identify associations between signaling and vaccine response categories in the elderly cohort. Samples from vaccine hyporesponders showed decreased IFNα-induced JAK/STAT pathway activity in B cells ($p<0.05$). IFNα responses in B cells were significantly lower in elderly compared with younger donors ($p<0.05$), suggesting that age-associated SCNP readouts may have clinical utility in predicting vaccine hyporesponse. These data support the potential utility of SCNP to: (1) identify elderly donors less likely to respond to vaccination, (2) provide a greater understanding of the immunological mechanisms underlying vaccine response and lack thereof, and (3) suggest novel targets for vaccine adjuvant development.

Biography

Diane Longo received her Ph.D. in Bioengineering at the University of California, San Diego, where her research concentrated on the role of autoregulation in signaling dynamics. In August 2009, Diane joined Nodality, a South San Francisco-based biotechnology company focused on the biological characterization of signaling pathways in patients with cancer and autoimmune diseases to enable more effective therapeutics development and decision-making.