The extracellular matrix as an immunomodulator

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The need for novel immunomodulators will increase as vaccines are developed using highly purified recombinant or synthetic peptide antigens that are safer and elicit specific immune responses. These new vaccines are generally less broadly immunogenic and therefore need adjuvants to enhance their immunogenicity. Several adjuvants are being developed to overcome real and perceived disadvantages of classical mineral salt adjuvants. One such adjuvant is the extracellular matrix (ECM). Experiments utilizing bacterial antigens have demonstrated that the ECM can potentiate the immune response of mice to these antigens.

For example, Balb/c mice were inoculated with Tetanus Toxoid (TT), TT + Alum (Alhydrogel), or TT + ECM with a boost 5 weeks later. After an additional 5 weeks, the animals were challenged with tetanus toxin and observed for neurotoxicity and mortality. In similarly vaccinated, unchallenged mice blood was collected at weeks 6 and 11 and ELISAs were performed to determine antibody titers and isotype ratios.

All animals inoculated with either TT + Alum or TT + ECM survived challenge with the Tetanus toxin compared to 70% survival when the animals were inoculated with TT alone. All controls succumbed to challenge. Serum titers after immunological boosting showed that ECM was more effective than Alum in inducing immune titers to the TT antigen. Lastly, isotyping the anti-TT antibodies demonstrated that Alum induced a Th2-polarized humoral response, while ECM has a Th1-polarized humoral response.

This evidence suggests that ECM may be a viable alternative to mineral salt adjuvants, with a different mechanism of action, and without the associated adverse effects.