THE ROLE OF POSTTRANSLATIONAL MODIFICATIONS OF MICROVESICLES IN SYSTEMIC IMMUNE RESPONSES OF MICE

Katalin É. Szabó-Taylor, Krisztina Pálóczi, Tamás Géza Szabó, Andrea Németh, Xabier Osteikoetxea, Barbara Sódar, Marianna Csilla Holub, Erna Pap, Bence György, Éva Pállinger, Mária Pásztói, Edit I. Buzás

Dept. Genetics, Cell- and Immunobiology, Semmelweis University, Budapest, Hungary

Introduction

Posttranslational protein modifications are considered to play an important role in orchestrating immune responses. However, there is very limited information on how posttranslational modifications of extracellular vesicles impact the immunogenicity of these structures.

The goal of our study was to assess immune responses of mice immunised with either native or posttranslationally modified microvesicles (MVs).

Methods

Murine Th1 T cell hybridoma (5/4E8) cells were used as a source of MVs. The secreted MVs were isolated by differential centrifugation and gravity driven filtration. Groups of mice (n=5/each group) were immunised subcutaneously with a stable emulsion of complete Freund's adjuvant and MVs (native, citrullinated (citMVs), deglycosylated (dgMVs) or oxidised MVs (oxMVs)). Total blood plasma IgM and IgG levels were measured by ELISA. Isolated MVs with/without post-synthetic modifications were used as recall antigens to stimulate draining lymph node cell cultures of mice immunised with the respective antigens.

Results

Total IgM and IgG antibodies of mice immunised with either native MVs or dgMVs, did not differ from those in the controls. In contrast, we found significantly elevated total IgM and IgG levels in sera of mice immunized with ox MVs ($p<0.05$ and $p<0.01$, respectively). Furthermore, total IgG but not IgM levels of mice immunised with citMVs was significantly elevated ($p<0.05$) as compared with adjuvant controls. In lymph node cells cultures, *in vitro* re-stimulation with dgMVs induced a more than two-fold elevation in IL-2 expression, while restimulation with autologous MVs, ox MVs and citMVs did not have an effect.

Conclusions

The elevated Ig levels induced by the immunisation with autologous oxMVs may reflect the reported immune anti-oxidant function of natural autoantibodies. Moreover, our data suggest that postsynthetic modifications of MVs (such as deglycosylation) may result in breaking T cell tolerance.

elméleti

poszter