TETRASPANINS DISPLAYED IN RETROVIRUS-DERIVED VIRUS-LIKE PARTICLES AND THEIR IMPACT IN VACCINE DEVELOPMENT

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Virus-like particles (VLPs) are a particular subset of subunit vaccines which are currently explored as safer alternatives to live attenuated or inactivated vaccines. Retroviruses have been widely explored as vectors for gene therapy and as scaffolds for vaccine candidates. One of retrovirus-like particles (retroVLPs) most attractive characteristic is their ability to incorporate heterologous envelope proteins, known as pseudotyping, as a mean to manipulate tropism or to present foreign antigens. As pseudotyping is a non-selective process, host cellular proteins are also included in retroVLPs membrane [1]. Many studies have addressed the identity of these host-proteins for particle characterization nevertheless, the contribution of host-proteins in retrovirus immunogenicity remains unclear. Moreover, patients infected with HIV and HCV are known to develop autoantibodies targeting self-proteins. As the origin of these autoantibodies is still unclear, the adventitious nature of host–derived proteins present in retroVLPs cannot be discarded.
Tetraspanins, in particular CD81, are amongst the most abundant host-proteins present in retrovirus membrane. Here we analyzed (i) the immunogenicity of tetraspanins in retroVLPs produced in xenogeneic cells (ii) the influence of CD81 in the diversity of host-proteins incorporated in retroVLPs and (iii) the impact of CD81-depletion in developing a retroVLPs-based HCV vaccine candidate.
Our results suggest tetraspanins are major immunogens present in retroVLPs. We show that CD81 is highly incorporated in retroVLPs produced in HEK293 cells inducing strong antibody and T-cell immune response in mice. Our results also show an increased diversity of tetraspanins in retroVLPs after CD81 depletion from producer cells with preservation of the overall immunogenic profile of retrovirus particles [2]. We further explore the impact of CD81 depletion on the development of a retroVLPs-based HCV vaccine candidate and we observe that HCV E2 incorporation on retroVLPs is directly affected by CD81 expression, thus diminished in CD81-negative retroVLPs.
These results highlight the dynamic and non-innocuous nature of host-derived proteins present in retroVLPs membrane. We consider this dynamic nature and its impact in product quality as an additional feature to be considered when developing retrovirus-based biopharmaceuticals.

References:
[1] Segura, M.M., et al., (2008) J Virol. 82(3): p. 1107-17
[2] H. R. Soares, *et al*. (2016) Vaccine. *(in press)*

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