Wiskott-Aldrich syndrome protein (WASP) is a novel interaction partner of HTLV-1 p8 and may contribute to p8 transfer between cells

Kemeter LM*, Millen S[1]*, Donhauser N[1], Hampe S[1], Kohrt S[1], Socher E[2,3], Sticht H[2], Thoma-Kress AK[1]

[1] Institute of Clinical and Molecular Virology, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Erlangen, Germany;
[2] Division of Bioinformatics, Institute of Biochemistry, FAU, Erlangen, Germany.
[3] Chair of Functional and Clinical Anatomy, Institute of Anatomy, FAU, Erlangen, Germany
*contributed equally

Background:
The Human T-cell leukemia virus type 1 (HTLV-1) orf I-encoded accessory protein p8 induces cellular protrusions which facilitate p8 and HTLV-1 transfer to target cells. We recently showed that vasodilator-stimulated phosphoprotein (VASP), a promoter of actin filament elongation, is crucial for p8 transfer and HTLV-1 transmission. In this study, we aimed to identify additional actin regulators to further elucidate the transfer of p8 between cells, since VASP was shown to be crucial for membrane recruitment of p8, but only to a lesser extent, for p8-induced protrusion formation.

Methods:
Bioinformatics, confocal imaging, and co-immunoprecipitation (co-IP), gene editing.

Results:
Putative interactions of p8 with Wiskott-Aldrich syndrome protein (WASP) were predicted by bioinformatics. WASP controls the activation of the Actin Related Protein 2/3 complex, which assembles actin filaments and therefore promotes elongation. A partial co-localization between WASP and p8 in Jurkat T-cells could be observed via immunofluorescence analysis. We confirmed that p8 interacts with WASP in 293T and Jurkat T-cells using co-immunoprecipitation. Since WASP is known to complex with VASP, a direct interaction partner of p8, and the interaction of p8 and WASP was progressively diminished in presence of increasing amounts of the detergent N-octylglucoside, our data suggested an indirect interaction of p8 and WASP via VASP. However, co-immunoprecipitations revealed that p8 still interacted with WASP upon knockout or knockdown of VASP in Jurkat and 293T cells, respectively, indicating that VASP is not required for formation of p8:WASP complexes. Moreover, precipitation of WASP was significantly diminished upon co-expression of p8, but not upon knockout of VASP suggesting that endogenous VASP competes with p8 for WASP binding.

Conclusion:
Together, our work identifies WASP as a new interaction partner of p8, which interacts with p8 independent of VASP and might be important for p8 transfer between cells.

Disclosure of Interest Statement:
Nothing to declare.