Induction of the tumor marker Fascin by HTLV Tax-1 and Tax-2 is linked to alternative NF-κB signaling

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Background:
Transcriptional regulation of the actin-bundling protein and tumor marker Fascin is highly diverse depending on cell and tumor type. Previously, we discovered that Fascin expression is considerably enhanced in T-cells by the viral oncoprotein Tax-1 of human T-cell leukemia virus type 1 (HTLV-1), depending on classical NF-κB signaling. However, it remains unclear whether the non-oncogenic Tax-2 of the related HTLV-2 has the same effect.

Methods:
To address this, we performed luciferase assays, immunoblot, and qPCR, comparing Tax-1 and Tax-2 expressing T-cells.

Results:
We found that Tax-2, which was able to robustly, but less potently induce alternative NF-κB signaling compared to Tax-1, elevates Fascin expression only moderately in two different T-cell lines (Jurkat, Molt-4). However, both viral oncoproteins had a similar activation effect on a 1.6 kb fragment as well as on Tax-responsive elements present in the human *Fascin* promoter. Furthermore, by making use of different Tax1-/ Tax-2 chimeras, we observed a correlation between Tax-induced activity of the alternative NF-κB pathway and Fascin induction. While treatment with the second mitochondria-derived activator of caspase (SMAC)-mimetic AZD5582, a compound known to robustly activate alternative NF-κB signaling, did not induce Fascin, the combination of AZD5582 with activation of classical NF-κB signaling by Tax-2 significantly induced *Fascin* on transcriptional level.

Conclusion:
In conclusion, our data demonstrate that both classical and alternative NF-κB activity are necessary for strong Fascin induction by the viral Tax oncoproteins, shedding new light on the regulation of Fascin in T-cells and during viral transformation.

Disclosure of Interest Statement:
Nothing to declare.