THE ACTIN-BUNDLING PROTEIN FASCIN CONTRIBUTES TO HTLV-1-INDUCED LYMPHOMAGENESIS IN AN ATLL XENOGRAFT MOUSE MODEL

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Background:  
Adult T-cell leukemia/lymphoma (ATLL) is a severe malignancy with poor prognosis caused by persistent infection with the oncogenic retrovirus Human T-cell leukemia virus type 1 (HTLV-1). We previously found that the actin-bundling protein Fascin, a tumor marker crucial for metastatic dissemination in many types of cancer, is upregulated in HTLV-1-infected T cells, induced by the viral Tax oncoprotein, and important for invasion of ATLL cells. Here we asked whether Fascin also contributes to lymphomagenesis in vivo in a murine model of acute ATLL.

Methods:  
Small hairpin RNA (shRNA)-mediated gene repression; a preclinical model of acute ATLL in non-obese diabetic/severe combined immunodeficient/ interleukin-2 receptor common gamma chain knock-out (NSG) mice; immunohistochemistry; quantitative PCR (qPCR); migration assays.

Results:  
Upon knockdown of Fascin in human chronically HTLV-1-infected C91/PL cells (C91/PL/shFascin cells), injection of these cells into NSG mice led to tumor development independently of Fascin repression. However, compared to mice injected with control cells (C91/PL/shNonsense), lymphoma growth was significantly delayed in mice xenografted with C91/PL/shFascin cells, suggesting that Fascin suppression impaired tumor progression in vivo. Immunohistochemistry revealed that Fascin was present in tumors and metastases in control mice. qPCR confirmed repression of Fascin in the xenografted C91/PL/shFascin cells and in tumors ex vivo, while expression of HTLV-1 Tax was unaffected by Fascin knockdown. Mechanistically, migration assays in Jurkat control cells, compared to Fascin knock-out cells, revealed that T-cell migration is enhanced in the presence of Fascin. Finally, analysis of Fascin expression in ATLL patients showed that Fascin is significantly upregulated in patients with skin lesions.
**Conclusion:**
Together, our data highlight an important role of Fascin in lymphomagenesis in a murine model of aggressive ATLL, and suggest that Fascin also contributes to lymphoma dissemination in ATLL patients.

**Disclosure of Interest Statement:**
Nothing to declare.