

1012 **FIBROBLAST ACTIVATION PROTEIN REGULATES HUMAN NATURAL KILLER CELL MIGRATION**

¹Rachael Maynard*, ¹Allison Fitzgerald, ¹Apsra Nasir, ¹Eric Glasgow, ¹Sandra Jablonski, ²Pieter Van Der Veken, ¹Gray Pearson, ³Emily Mace, ¹Louis Weiner. ¹Georgetown University Medical Center, Washington, DC, United States; ²University of Antwerp, Wilrijk, Belgium; ³Columbia University Irving Medical Center, New York, NY, United States

Background Natural killer (NK) cells play a crucial role in both physiologic and pathologic conditions, including cancer. A number of strategies have been employed to utilize the cytolytic properties of NK cells in the treatment of cancer.^{1,2} One hurdle to the efficacy of NK-cell based therapy is NK cell infiltration into tumors.³ The mechanisms NK cells employ for physical migration are not well described.^{4,5} We recently found that fibroblast activation protein (FAP) is expressed by human NK cells. FAP is a type-II transmembrane serine protease previously thought to primarily be expressed in reactive stromal fibroblasts. FAP plays a role in tissue remodeling and extracellular matrix digestion to facilitate cell migration.⁶

Methods FAP expression was examined on NK cells by both western blot and immunofluorescence. Compound 60 (CDP60) was used as a specific pharmacological inhibitor of FAP in these assays.

Results We have confirmed that fibroblast activation protein (FAP) is expressed by human NK cells, using both western blot and immunofluorescence. To examine the role of FAP in NK cells we find that following inhibition of FAP activity, NK cells demonstrate decreased migration in 3D culture systems, as well as decreased extravasation from the blood vessels of zebrafish.

Conclusions Future studies include generating an FAP knock-out NK cell line to verify the role of FAP in NK cells identified using CPD60. These findings suggest that FAP is responsible for NK cell migration and may provide a potential novel mechanism to regulate this process. This role in migration can potentially be exploited to enhance NK cell migration into tumors.

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