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Junctional adhesion molecules mediate transendothelial migration of dendritic cell vaccine in cancer immunotherapy

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ABSTRACT

In vitro **generated dendritic cells (DCs) have been studied in cancer immunotherapy for decades. However, the detailed molecular mechanism underlying transendothelial migration (TEM) of DC vaccine across the endothelial barrier to regional lymph nodes (LNs) remains largely unknown. Here, we found that junctional adhesion molecule (JAM)-Like (JAML) is involved in the TEM of mouse bone marrow-derived DCs (BMDCs). Treatment with an anti-JAML antibody or JAML knock-down significantly reduced the TEM activity of BMDCs, leading to impairment of DC-based cancer immunotherapy. We found that the interaction of JAML of BMDCs with the coxsackie and adenovirus receptor of endothelial cells plays a crucial role in the TEM of BMDCs. On the other hand, human monocyte-derived DCs (MoDCs) did not express the JAML protein but still showed normal TEM activity. We found that MoDCs express only JAM1 and that the homophilic interaction of JAM1 is essential for MoDC TEM across a HUVEC monolayer. Our findings suggest that specific JAM family members play an important role in the TEM of *in vitro*-generated mouse and human DCs from the inoculation site to regional LNs in DC-based cancer immunotherapy.**

Keywords: Mouse bone marrow-derived dendritic cells (BMDCs), human monocyte-derived dendritic cells (MoDCs), TEM, JAM, JAML, DC immunotherapy