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Integrin $\alpha\beta6$: structure, function and role in health and disease

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Running title: Integrin $\alpha\beta6$ in health and disease

Abbreviations: DC, dendritic cells; EBV, Epstein–Barr virus; ECM, extracellular matrix; EGFR, epidermal growth factor receptor; EMT, epithelial-to-mesenchymal transformation; ERK, extracellular signal-regulated kinase; FMDV, foot-and-mouth disease virus; HSV, herpes simplex virus; LAP, latency-associated peptide; MMP, matrix metalloproteinase; STAT3, signal transducer and activator of transcription 3; TGF- β , transforming growth factor- β ; TolBC, tolerogenic B cell; Treg, regulatory T cell; Trm, tissue-resident memory T cell; uPA, urokinase-type plasminogen activator

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Abstract

Integrins are cell surface receptors that traditionally mediate cell-to-extracellular matrix and cell-to-cell adhesion. They can, however, also bind a large repertoire of other molecules. Integrin $\alpha\beta6$ is exclusively expressed in epithelial cells where it can, for example, serve as a fibronectin receptor. However, its hallmark function is to activate transforming growth factor- $\beta1$ (TGF- $\beta1$) to modulate innate immune surveillance in lungs and skin and along the gastrointestinal tract, and to maintain epithelial stem cell quiescence. The loss of $\alpha\beta6$ integrin function in mice and humans leads to an altered immune response in lungs and skin, amelogenesis imperfecta, periodontal disease and, in some

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