学 位 論 文 の 要 旨

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主論文の題名

Irisin supports integrin-mediated cell adhesion of lymphocytes

主論文の要旨

Irisin, a myokine released from skeletal muscle, has recently been found to act as a ligand for the integrins αVβ5, αVβ1, and α5β1 expressed on mesenchymal cells, thereby playing an important role in the metabolic remodeling of the bone, skeletal muscle and adipose tissues. Although the immune-modulatory effects of irisin in chronic inflammation have been documented, its interactions with lymphocytic integrins have yet to be elucidated. Here, we show that irisin supports the cell adhesion of human and mouse lymphocytes. Cell adhesion assays using a panel of inhibitory antibodies to integrins have shown that irisin-mediated lymphocyte adhesion involves multiple integrins including not only α4β1 and α5β1, but also leukocyte-specific αLβ2 and α4β7. Importantly, mouse lymphocytic TK-1 cells that lack the expression of β1 integrins have exhibited αLβ2- and α4β7-mediated cell adhesion to irisin. Irisin has also been demonstrated to bind to purified recombinant integrin αLβ2 and α4β7 proteins. Thus, irisin represents a novel ligand for integrin αLβ2 and α4β7, capable of supporting lymphocyte cell adhesion independently of β1 integrins. These results suggest that irisin may play an important role in regulating lymphocyte adhesion and migration in the inflamed vasculature.