

Medicinal Chemistry & Computer Aided Drug Designing

November 02-04, 2015 Atlanta, USA

Irisin as a performed monomer for adipocyte browning

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Exercise has well-recognized beneficial effects on system metabolism. Irisin was recently identified as an exercise-induced peptide hormone secreted by skeletal muscle in mice and humans. The hormone is thought to bind to so far unidentified surface receptor on white fat cells and induces “browning” effects that improve the tissue metabolic profile and increase whole-body energy expenditure. As a potential new anti-obesity and anti-diabetes target, this peptide hormone is however poorly characterized. We have successfully manufactured recombinant irisin, which provides a key reagent for detailed biochemical, biophysical, and pharmacological characterizations. Wild type irisin exists in the form of dimer in solution. Through structure-based computational modeling and systematic surface mutagenesis, we have mapped out the detailed dimeric interface and engineered monomeric irisin variants. The interface is consistent with what was identified by X-ray crystallography. Several monomeric irisin variants have been engineered and identified. Circular dichroism analyses suggest marked differences comparing monomer variants to dimer variants. A sensitive adipocyte-based functional assay has been established in our laboratory. Based on the cell-based functional assay and signaling activation assay, we identified several active monomeric variants including a highly active monomer variant. A model of how irisin molecule activates adipocyte browning program has been proposed.

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