

S-J Lee Nomination for Luft prize

Se-Jin Lee's major scientific contributions are the discovery of myostatin and the elucidation of its function as a key regulator of skeletal muscle mass. Lee's work has provided important insights into the control of tissue growth, and has stimulated extensive efforts to exploit this signaling pathway in combating muscle loss.

Lee identified myostatin as a new, muscle-specific member of the transforming growth factor- β superfamily. With his student (Alexandra McPherron), he showed that mice engineered to lack myostatin develop muscles more than twice the normal size, demonstrating that myostatin normally acts to limit skeletal muscle mass. Lee went on to elucidate the molecular mechanisms underlying this effect, identifying the following: naturally-occurring myostatin mutations in cattle (with Alexandra McPherron and concurrently with others) and humans (with Markus Schuelke); myostatin receptors; naturally-occurring inhibitory binding proteins (including follistatin and the myostatin propeptide); and myostatin inhibitors capable of increasing muscle growth *in vivo* (with Neil Wolfman). Lee's discoveries have not only uncovered a fundamental mechanism by which muscle mass is controlled, but also revived an archaic theory about the regulation of tissue size by growth inhibitors dubbed chalone. Specifically, Lee's work has demonstrated that myostatin is a muscle chalone, providing the first clear example of this regulatory mechanism. In addition to being highly significant in its own right, the discovery of myostatin has launched a widespread effort to target this pathway for both agricultural and human therapeutic applications. Lee's laboratory has contributed greatly to demonstrating the beneficial effects of myostatin inhibition in models of muscle degenerative and metabolic diseases—findings that have resulted in at least four biotechnology and pharmaceutical companies initiating clinical trials with myostatin inhibitors for the treatment of patients with debilitating muscle loss. Importantly, positive results from early human trials have been reported.