Signal Integration

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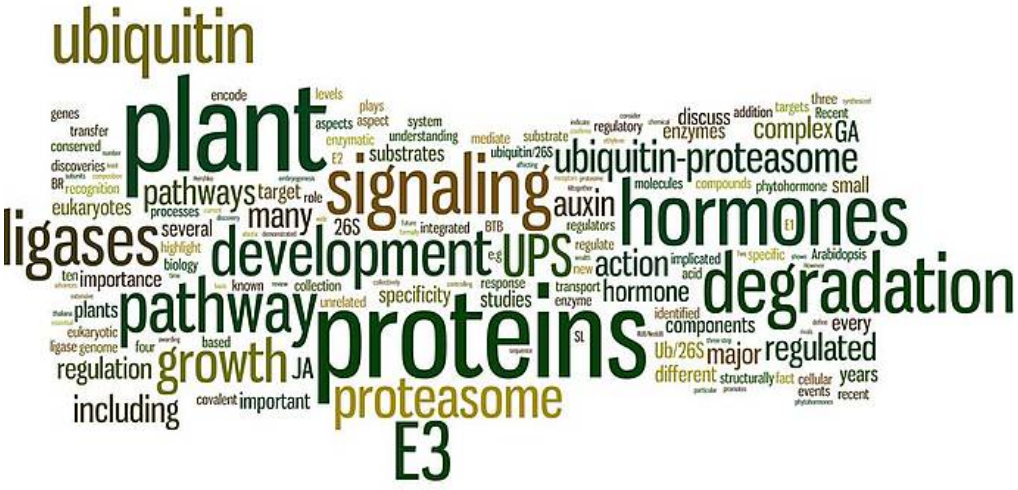

Groundbreaking findings constitute the basis for the *Signal Integration Group* as SKP1/CDC53/F-Box protein, (SCF)-type E3 complexes, $SCF^{TIR1/AFB1-5}$ and their degradation targets, the short-lived AUX/IAA transcriptional repressors, were shown to form an auxin co-receptor system. Thus, distinct TIR1/AFB-AUX/IAA co-receptor pairs are differentially perceptive to auxin and constitute various auxin sensors *in vivo* (Tan, X. *et al. Nature* 2007, Calderón Villalobos, L.I.A., *et al. Nat Chem Biol* 2012). The evidence that SCFs consolidate protein degradation, small molecule perception, and cofactor regulation suggests they act as SIGNAL INTEGRATORS essential for growth and development of plants.

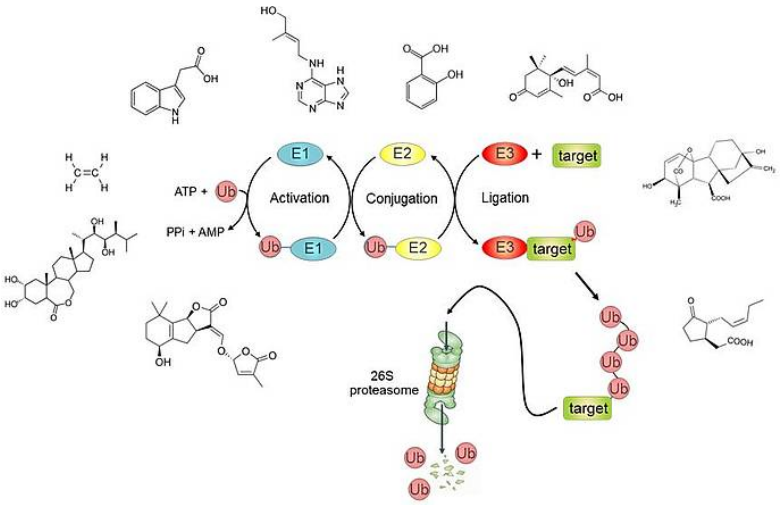

Figure 1: Through an E1-E2-E3 enzymatic cascade eukaryotic cells label turnover-regulated proteins with a polyubiquitin chain, which serves as a targeting signal for the proteasome. E3-Ub ligases specifically and directly interact with the degradation substrates.

Our general research plan is designed to characterize small molecule perception through protein stability mechanisms, and, in the long term, to uncover roles for small molecule interactions in specific plant responses and developmental programs.

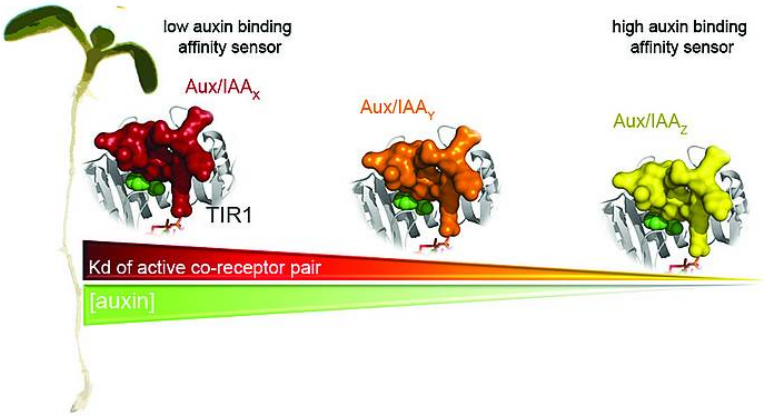

Figure 2: Different Auxin Co-Receptor Complexes ($SCF^{TIR1/AFBs}$:AUX/IAAs) Continuously Assess Auxin Levels (from graphical abstract, Calderón Villalobos, L.I.A. *et al*, (2012) *Nat Chem Biol* 8, 477-485

To understand mechanistically the assembly and regulation of SCF-type E3s-substrate systems, we use initially the TIR1/AFB-InsP6-auxin-Aux/IAA model. We are specifically: 1) analyzing functionally auxin signal sensors *in vivo*, and characterizing the dynamics, regulation and structure-function of hormone sensors; 2) establishing the role of SCF regulators, such as phosphoinositide cofactors, on TIR1/AFB function.

To pursue our general goal of contributing to the understanding of biological mechanisms mediated by protein-degradation, we are also focusing on: 3) profiling of SCF-type E3s substrate, and SCF-type E3s/small molecule interactions in plants, and 4) designing strategies to track small molecule-dependent protein turnover *in vivo*.

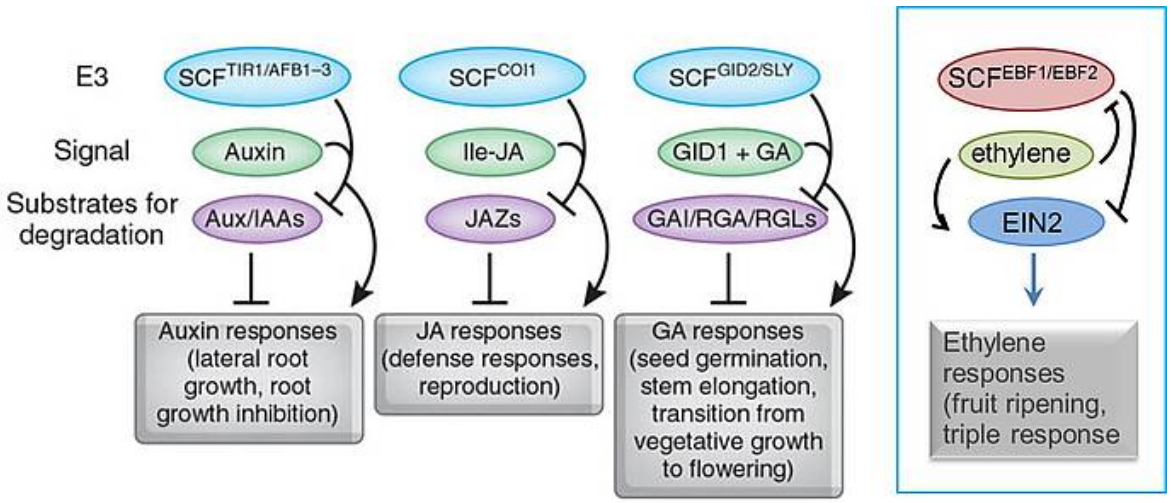

Figure 3: SCF-E3–type Ubiquitin Ligases Promote the Ubiquitination and Degradation of Repressors of Auxin-, JA- and GA-regulated Transcription, And of Activators of Ethylene-dependent TFs. Modified from Santner, A., Calderón Villalobos L.I.A, Estelle, M. (2009) *Nat Chem Biol* 5(5):301-7