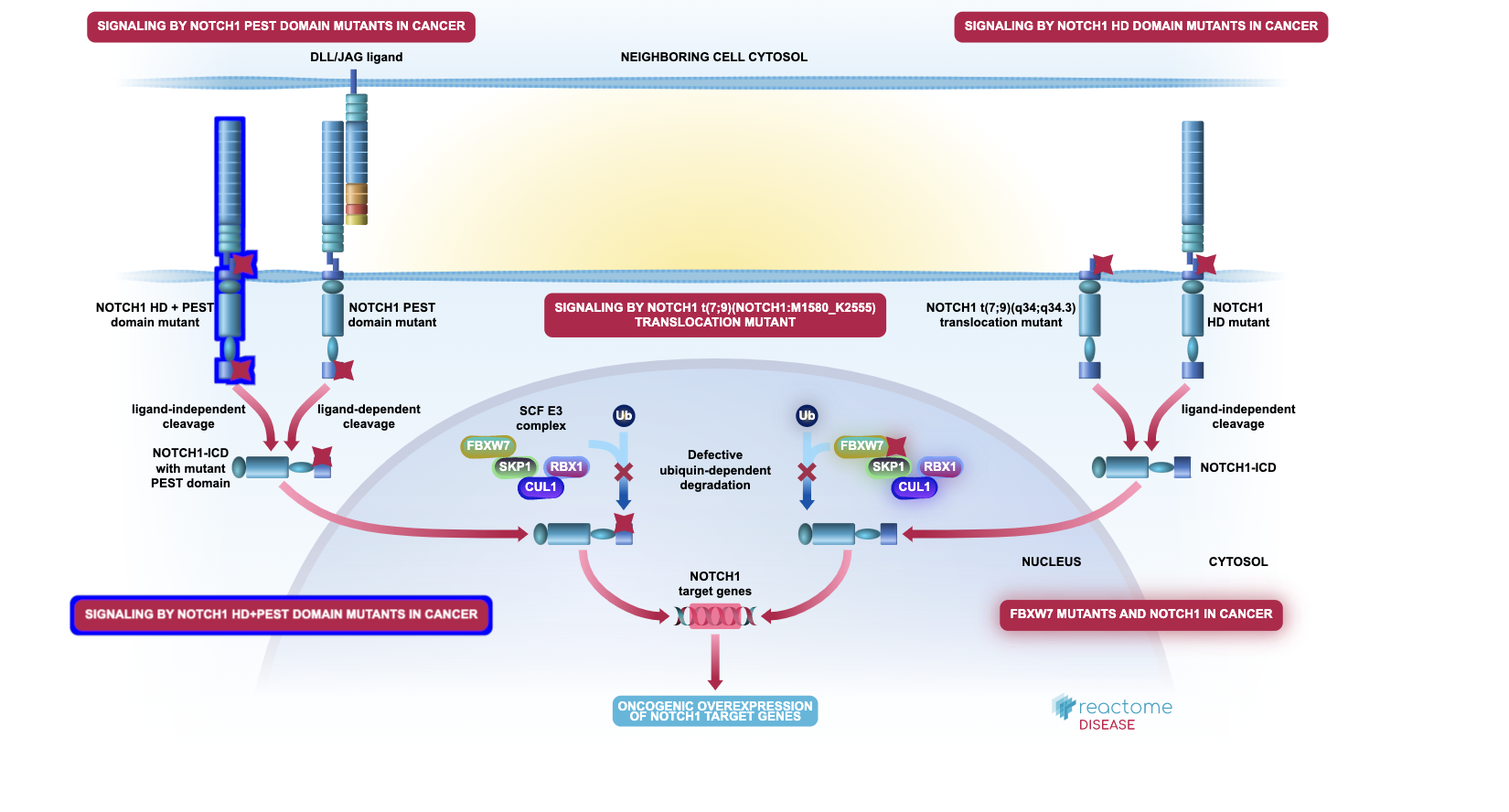
**Identify a signal transduction pathway that results in a specific disease and share this in a post to the class**

NOTCH1 gene provides instructions for making the receptor protein Notch1. Attachment of a ligand to the Notch 1 receptor, sends signals important in embryonic development, cell-to-cell interaction; they regulate cell growth, differentiation, division and apoptosis. Notch1 is involved in many types of cancers, including brain cancers, breast cancers and leukemias. NOTCH1 can act as oncogene and a tumor suppressor. T-cell acute lymphoblastic leukemia (T-ALL) is an acute bone marrow cancer, accounting for ~20% of acute lymphocytic leukemia (ALL), for which survival outcomes have not changed significantly for last 30 years.

Mutations in the PEST (Proline, Glutamic acid, Serine, and Threonine sequence acts as a signal peptide for protein degradation) and heterodimerization (HD) domains of NOTCH1 have been present in more than 50% of T-ALL patients which is indicated in *“overall signaling by NOTCH1 in Cancer”* diagram. These mutations interfere with ubiquitination-mediated NOTCH1 downregulation and lead to defective ubiquin-dependent degradation, increasing g NOTCH1 transcriptional activity by 40-fold.

γ-secretase inhibitors (GSIs) to inhibit NOTCH1 signaling have faced many challenges including gastrointestinal adverse effects, other strategies like combined therapies or small molecules are currently investigated.



What else did you find interesting or useful about this database?