Test scenario for Module 1: Retriving articles based on relevant interactions and concepts

**Problem:** *GAB2* is located at 11q14.1, a chromosomal region that has not been implicated before in Alzheimer’s Disease (AD) in genome-wide linkage or association studies. *GAB2* is a scaffolding protein in numerous growth and differentiation signaling pathways, including MAPK/Akt and PI3K, and may be involved in inversely modulating the hyperphosphorylation of tau, a core pathological feature of AD. In fact, reduction of *GAB2* expression was shown to increase tau phosphorylation in vitro [Reiman et al., 2007].

Interestingly, in peripherally related articles two other key proteins in the pathological cascade leading to AD (amyloid precursor protein (APP, also called APOE) and presenilin 1 (PSEN1)) interact with the GRB2 adaptor protein to modulate ERK1,2 signaling [Nizzari et al., 2007; Russo et al., 2002].

GRB2 is important because it binds to the proline rich domain in GAB2 and is thought to mediate recruitment of GAB2 to receptor tyrosine kinases [Li et al, 2004].

Chapuis et al (2008), however, claim little if any association of GAB2 alleles with Alzheimer’s disease regardless of APOE allele status [Chapuis, J et al, 2008].

**Task:** You want to see if you find anything else in the research literature linking *GAB2* to AD or suggesting a credible and plausible biological story for the association. The question driving this exploration is:

*What other papers beside the ones cited above are available that suggest or refute an association between *GAB2* and Alzheimer’s disease in humans?*

Ideally, you want to find literature you wouldn’t find with your usual means of searching

- You will follow leads to articles suggested by interactions that *GAB2*, GRB2 and other relevant genes are known to have.
- You may find articles published earlier than you usually examine
- You may find articles from other subspecialties than your own.
- You may find articles from other organisms.