

Test scenario for Module 1:

Retrieving 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:

The main 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.