Protein-protein interactions

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What are proteins?

• Biological machines that perform all sorts of functions
• Estimated 0.25-1 million different proteins in the human body
How do we know what proteins look like?

X-ray crystallography

- Purify protein
- Make into crystal
- Shoot X-rays through it
- ???
- Profit!

Simulation

- We know what affects structure: Hydrogen bonds, disulfide bridges, ionic interactions, hydrophobicity, Van der Waals forces...
- So we simulate it!
- [https://folding.stanford.edu/](https://folding.stanford.edu/)
Where do I find pretty pictures of proteins?

- Protein Data Bank (www.rcsb.org/)

Protein-protein interactions

- Why do we care?
How do we identify interactions?

- Experiments!
- Tons of ways I don’t know anything about, but you can read about it on Wikipedia

How do we get the big picture?

- Text mine the literature!
AIMS:
We herein investigated the inducibility of cytochrome P450 1A1 (CYP1A1) by Δ⁶-tetrahydrocannabinol, cannabidiol (CBD), and cannabinol, three major phytocannabinoids, using human hepatoma HepG2 cells.

MAIN METHODS:
The expression of CYP1A1 and the aryl hydrocarbon receptor (AhR) was measured by quantitative real-time polymerase chain reaction and/or Western blotting.

KEY FINDINGS:
Δ⁶-Tetrahydrocannabinol and CBD concentration-dependently induced the expression of CYP1A1 mRNA, whereas cannabinol showed little or no induction. Among the phytocannabinoids tested, CBD was the most potent inducer of CYP1A1 expression. The induction of CYP1A1 expression by CBD was significantly attenuated by the knockdown of AhR expression with AhR small interfering RNAs. The role of protein tyrosine kinases (PTKs) in the CBD-mediated induction of CYP1A1 was then examined using herbimycin A, a PTK inhibitor. The upregulation of CYP1A1 by CBD was significantly suppressed by herbimycin A as was the induction by omeprazole but not 3-methylcholanthrene. The inducibility of CYP1A1 by CBD-related compounds was examined to clarify the structural requirements for CBD-mediated CYP1A1 induction. Olivetol, which corresponds to the pentyresorcinol moiety of CBD, significantly induced the expression of CYP1A1, whereas d-limonene, CBD-2’-dimethyl ether, and CBD-2’-6’-dimethyl ether did not.

SIGNIFICANCE:
These results showed that CBD may have induced human CYP1A1 expression through the activation of PTK-dependent AhR signaling, in which two phenolic hydroxyl groups in the pentyresorcinol moiety of CBD may play structurally important roles.

Text mining methods

- Natural Language Processing
- Things we care about: Co-occurrence of terms, negation, semantics, vagueness...
- Natural language is hard!

Okay, we mined a bunch of PPIs. Now what?

- Do Science!
- Check to see if predicted interactions are real by doing experiments
- Learn about biochemical pathways you didn’t know before
- Find drugs that affect these pathways and use them to cure disease
## Visualization

- Draw interactions in a graph: The interactome
- [http://www.cytoscape.org/](http://www.cytoscape.org/)

## Protein-protein interaction resources