Practical Bioinformatics

Wagner Section

Exercise Block 5. You are involved in an international effort to design a drug that would stop the spread of enterohemorrhagic *E. coli* Sakai. You want to develop a drug that kills *E. coli* Sakai strains, but not the commensal *E. coli* MG1655 strain.

You have models of the metabolic networks of the following two organisms: iEco1339_MG1655 and iEco1345_Sakai. How would you tackle this problem?
Here are some ideas of analyses you can perform. We encourage you to also try your own ideas.

Exercise 5.1. Start by comparing growth rates of MG1655 and Sakai in a glucose-minimal environment in aerobic and anaerobic conditions. What is your explanation for the observed differences between the strains?

Different *E. coli* strains grow in different environments, wherein certain nutrients may be available at different concentrations. Different strains may also import nutrients at different rates. Baumler *et al*. (http://www.biomedcentral.com/1752-0509/5/182) measured glucose uptake rates for three strains of *E. coli* in aerobic and anaerobic environments (see table below).

	Glucose uptake rate (mmol/gDW/h)	
Strain	Aerobic	Anaerobic
E. coli MG1655	15.5	8.1
E. coli Sakai (EHEC)	7.9	19.2

Use the experimentally determined glucose uptake rates to construct the minimal glucose medium. A list with all the other metabolites needed for the minimal environment can be found in template_minimal_env.txt, the uptake rate of which should be set to 1000.

Exercise 5.2. It could also be useful to know if the strains grow on different carbon sources. Explore this.

Set the environment to include only the (non-carbon-containing) metabolites listed in template_minimal_env.txt. Then add each carbon source listed in the file carbon_source_list.txt individually and determine the organisms' growth.

Exercise 5.3. Suitable drug target(s) would involve reactions that are essential specifically in the Sakai strain. Only if such reactions are identified will the chemists in your team be able to synthesize a drug that kills the EHEC strain specifically. On a glucose-minimal medium, how many such drug targets are there?

Exercise 5.4. Compare the full list of reactions of the *E. coli* strains Sakai and MG1655. Where do they differ? Can you find reactions that are in some way related to the pathogenicity of the Sakai strain?

Exercise 5.5. Could the drug targets you proposed for Sakai also (fortuitously) be potential drug targets in the other strains on a glucose-minimal medium?

Study the effect of the drug on the following metabolic networks:

iEco1339_MG1655 – Metabolic network of the *E. coli* MG1655 strain, a common laboratory strain
iEco1288_CFT073 – Metabolic network of the *E. coli* CFT073 strain, a pathogen of the urinary tract
iEco1344_EDL933 – Metabolic network of the *E. coli* EDL933 strain, an enterohemorrhagic pathogen
iEco1301_UTI89 – Metabolic network of the *E. coli* UTI89 strain, another pathogen of the urinary tract
iEco1335_W3110 – Metabolic network of the *E. coli* W3110 strain, another laboratory strain