**Practical Bioinformatics**

Wagner Section

**Exercise 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 for the metabolic networks for these 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.

**5.1. Start by comparing growth rates of MG1655 and Sakai in 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). Use the experimentally determined glucose uptake rates to construct the minimal glucose medium. A list with all the metabolites needed for the minimal environment can be found in template\_minimal\_env.txt.

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

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

The file carbon\_source\_list has a list of carbons sources that can be imported by the strains.

**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 EHEC strain specifically. How many such drug targets are there?**

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

**5.5. Could the drug targets you proposed for Sakai also (fortuitously) be potential drug targets in the other strains?**

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.

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.