3) **Propose an approach to identify lead compounds for a drug that you plan to develop.**

**Due date: Mon, Nov 21, 2005**

As a third part of your project, you are expected to come up with a plan how to identify potential drug candidates for the disease you are working on. If you have a validated target, this typically means development of a specific biochemical, cell-based, or *in silico* assay. If you follow "chemical genomic" route, this would mean development of high-throughput cell-based screening methods.

Please discuss what the rationale behind using such an assay is and identify any potential limitations. Your assay can be either molecular-biology based (e.g. quantification of particular mRNA using molecular beacons), biochemical (e.g. measuring ligand binding to the receptor), cell-based (e.g. monitoring the formation of a fluorescent reaction product in live cells), histological (analysis of tissue appearance), clinical (determination of viral load), or end-point assay (improvement in host health).

The lecture material should give you a good starting point and may be sufficient in simple scenarios, such as in vitro identification of inhibitors for alcohol dehydrogenase. You most likely need to work with scientific literature in order to best to decide which particular approach is most appropriate. Original research papers also allow you to learn more about details of specific assays. However, you do not need to hunt down the original research in which the assay was developed or applied to your target. For some more pioneering projects such papers may not simply exist; it is sufficient that you provide evidence that a particular assay or animal model is appropriate to your target and disease.

Keep in mind that we are not talking about human clinical trials here yet but at most well-characterized animal models of the disease.

You may propose virtual screening as your assay if the structure of your validated target is known and available. The advantage of this approach is that you are actually able to carry out the virtual screening using the Schrödinger software suite. We will be covering the relevant background soon in the class. However, be aware that if you propose virtual screening as your approach, you need to submit preliminary evidence about the feasibility of this at the end of this quarter; if you go on taking Chem162B you are expected to actually carry out a small-scale virtual screening against your target.