Lesson 11

Final Project Startup
Final Project

- From sequence to model
  - HA or NA

- Biological question
  - Vaccine design
  - Drugs
  - Escape mutants

- Choose sides!
  - Virus versus human

- Poster
  - Presentation
Final Project Assessment

- Group poster presentations
  - All group members present the work and answer questions.

- Question for another group (buddy group)

- Individual oral exam starting from posters
  - May 9th and 16th.
  - (Or possibly 16th and 23rd).
"Coming together is a beginning, keeping together is progress, working together is success".

Henry Ford
During the whole development of the space program, Larry had not contributed with anything whatsoever, and he knew that this was his absolutely last chance. Stop! Stop! Don't just push the button! Ehnh… Count down first! Yes! Countdown! That's a good idea! Otherwise it will never make it to the Moon! Never!
Group Work & Rules

- Define your group
  - 2-4 members
- Establish a group name and a logo
- Discuss roles within your group based on the profiles of the individual members
- Agree on a written set of rules for:
  - Meetings
  - Conflict resolution
  - Decision making
  - Communication

Feed in potential conflicts
Feed in any good/bad group experiences
Handin of Project

- Deadline: Monday April 30th at noon!

- For printing posters: Small fee (?)
  - Exact amount to be announced on CampusNet.
  - Or print it yourself…
Project Contents
From Sequence to Hypothesis

- Simple homology modelling
  - Modelling with a template

- Fold recognition and other sequence predictions
  - Working without a template

- Presenting the model

- Generating a hypothesis

- Produce testable conclusions
Homology Modelling

- HHpred or CPHmodels
  - Single or multi-template models

- Selecting a template
  - The three Rs
  - Template versus model properties/biology
  - Model validation
    • ProQ, Anolea etc.
Sequence Features

- The template-less regions
  - Secondary structure
    - PsiPred
  - Signal peptide
    - SignalP
  - Transmembrane helices
    - TMHMM, Phobius
  - Modification sites
    - NetNGlyc
  - Intrinsic protein disorder
    - DisEMBL, IUpred
Model Overview

- Generate complete model
  - Multimers and crystal symmetry

- Show general properties
  - Secondary structure
  - Active site/binding pocket
  - Indicate missing parts
  - Modifications
    - Glycosylation, cleavage etc.
Generating a Hypothesis

- Decide on project goal
  - Drug design, virus evolution, vaccine design etc.

- Graft ligands into/onto model from real structures

- Analyse interactions
  - Site chain mutagenesis/reorientation
  - Drug modifications
  - Electrostatics (surfaces)
  - Sequence/structure conservation (ProtSkin)

- Suggest changes & propose outcome

- Take suggestions to a biologist/chemist 😊
Project Topics

- HA or NA

- Your Favourite Protein
  - Special projects (typically related to master thesis or Ph.D. work)

- All projects need my approval!
Articles

- See HA & NA folder on CampusNet under Reading material.

- If you are having trouble getting a paper, let me know, and I will do my best to get it for you.
Bird Flu Is Still Here…
And We Might Need New Drugs…

CDC Statement on Oseltamivir (Tamiflu®) Resistance and Antiviral Recommendations

For Immediate Release: January 9, 2009
Contact: CDC Division of Media Relations (media) - Phone: (404) 639-3286

On December 19, 2008, CDC issued interim guidance for health care professionals (http://www.cdc.gov/flu/professionals/antivirals/summary.htm) on the use of influenza antiviral medications (http://www.cdc.gov/flu/prof/antiviral/index.html) this flu season. The guidance was issued in response to early data from a limited number of states indicating that a high proportion of influenza A (H1N1) viruses are resistant to the influenza antiviral medication oseltamivir (Tamiflu®). Worldwide, the proportion of H1N1 viruses that are resistant to oseltamivir has been increasing so this development is not surprising.
Influenza Virus Basics

- Neuraminidase
- Hemagglutinin
- RNA
- M₂ protein (only on type A)
The Two Mechanisms whereby Pandemic Influenza Originates.

In 1918, an H1N1 virus closely related to avian viruses adapted to replicate efficiently in humans. In 1957 and in 1968, reassortment events led to new viruses that resulted in pandemic influenza. The 1957 influenza virus (Asian influenza, an H2N2 virus) acquired three genetic segments from an avian species (a hemagglutinin, a neuraminidase, and a polymerase gene, PB1), and the 1968 influenza virus (Hong Kong influenza, an H3N2 virus) acquired two genetic segments from an avian species (hemagglutinin and PB1). Future pandemic strains could arise through either mechanism.
## Influenza Virus Variants

<table>
<thead>
<tr>
<th>Year and Country</th>
<th>Virus</th>
<th>Designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995, United Kingdom</td>
<td>H7N7</td>
<td>A/Eng/268/95</td>
</tr>
<tr>
<td>1997, Hong Kong</td>
<td>H5N1</td>
<td>A/HK/156/97</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A/HK/148/97</td>
</tr>
<tr>
<td>1999, Hong Kong</td>
<td>H9N2</td>
<td>A/HK/1073/99</td>
</tr>
<tr>
<td>2003, Hong Kong</td>
<td>H5N1</td>
<td>A/HK/213/03</td>
</tr>
<tr>
<td>2003, the Netherlands</td>
<td>H7N7</td>
<td>A/Neth/33/03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A/Neth/219/03</td>
</tr>
<tr>
<td>2003, Hong Kong</td>
<td>H9N2</td>
<td>A/HK/2018/03</td>
</tr>
<tr>
<td>2004, Vietnam</td>
<td>H5N1</td>
<td>A/VN/1203/04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A/VN/1194/04</td>
</tr>
<tr>
<td>2004, Thailand</td>
<td>H5N1</td>
<td>A/Thai/16/04</td>
</tr>
<tr>
<td>2004, Canada</td>
<td>H7N3</td>
<td>NA</td>
</tr>
<tr>
<td>2004, Egypt</td>
<td>H10N7</td>
<td>NA</td>
</tr>
</tbody>
</table>

*H5 and H9 viruses have generally been associated with respiratory disease, whereas H7 has generally been associated with conjunctivitis. NA denotes not available.*
The Poster

- A0 (1189mm x 841 mm)
- 1/3 for figures
- 1000 words max.
  - Keep the introduction short
  - IMRAD
- Printing
Poster Session

- Meet at 8.00 AM in room 062

- Presentation
  - 15-20 minutes per group including questions/discussion.

- Buddy group questions
  - Each group member should formulate one key question to ask the buddy group at the poster session.

- Buddy groups will be announced on CampusNet one week before the poster session.
Oral Exam

- **The exam:**
  - Brief project presentation (3-4 minutes; from A4 print of poster).
  - Discussion of various aspects of your project. Questions can fall within any topic covered by the course curriculum.

- **NOTE:** *The total examination time including your presentation and grading is 20 minutes.*

- **Rules of thumb:**
  - Answer questions as briefly and concisely as you can.
  - Ask to have questions repeated or rephrased if you don't understand them.
  - In case you don't know the answer, ask for another question.

  - Do *not* expect to be corrected during the exam if you give wrong answers – it is better for our evaluation of you to ask another question.
Deliverables

- Project synopsis
  - Project title + 100 word (max.) summary
  - Mail to me: blicher@cbs.dtu.dk
  - Deadline: April 23rd (next Monday)

- Poster
  - Deadline: April 30th (Monday) @ noon.

- Buddy group questions
  - Deadline: May 2nd (at the poster session)
Important Dates

- Project synopsis

- Poster deadline:
  - Monday April 30th at noon!

- Exam dates:
  - May 9th + 16th (or 16th and 23rd)

- Course evaluation on CampusNet
  - April 23rd to April 30th
Exam Date Preferences

- If you have special preferences/needs regarding the exam date...

- May 9\textsuperscript{th} + 16\textsuperscript{th} (or 16\textsuperscript{th} + 23\textsuperscript{rd})
  - 8.00 AM to 5.00 PM in room 060.

- ... send me a mail (blicher@cbs.dtu.dk) with your preferred date and reason.