Introduction of Structural Biology Team

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Institute of Molecular Genetics

Academy of Sciences of the Czech Republic
# Structural biology team

**IOCB + IMG**

<table>
<thead>
<tr>
<th>Staff</th>
<th>Techniques &amp; equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 scientists</td>
<td>Gene cloning</td>
</tr>
<tr>
<td>2 postdocs</td>
<td>Recombinant expression <em>(bacterial + insect + human)</em></td>
</tr>
<tr>
<td>3 research assistants</td>
<td>Protein purification + characterization</td>
</tr>
<tr>
<td>2 technicians</td>
<td>Protein crystallization</td>
</tr>
<tr>
<td>3 graduate students</td>
<td>Protein crystallography</td>
</tr>
<tr>
<td>2 undergraduate student</td>
<td>NMR spectroscopy</td>
</tr>
</tbody>
</table>

Structure determination

Basic molecular modeling

Small-molecular crystallography
Structural biology team
IOCB + IMG

Techniques & equipment
Recent crystal structures

3T3C

4E1W

N/D

1NHD

3VBD

3FV3

3LDR

N/D

3T3C

3UNU

10KG

2HKF

318T

3T6G

N/D
Structure as tool: structure-base drug design

HIV protease

understanding HIV PR drug resistance

X-ray crystallography

X-ray data collection
structure determination

crystallization

Structure analysis:
inhibitor structure
inhibitor interactions
HIV PR structural changes
molecular dynamics etc.

Structure-based drug design

Human carbonic anhydrase
Human nucleotidase
Candida aspartic protease
Schistosoma cathepsin D
Structure as goal: structural biology

Cystatin
*Ornithodoros moubata*

Galectin-4
*Mus musculus*

JPO2 & PogZ transcription factors
*Homo sapiens*

Serpin-2
*Ixodes ricinus*

Transcription repressor AraR
*Bacillus subtilis*

C-terminal LEDGF
*Homo sapiens*
DNA → cloning → expression → purification

DNA → crystal growth → cryo-preservation

DNA → data collection →

\[ \rho(x,y,z) = \frac{1}{V} \sum_{h,k,l} \left| F_{hk0} \right|^2 e^{-2\pi i (hx + ky + lz)} \]

DNA → data analysis →

DNA → final model
Proteins from structural genomics

<table>
<thead>
<tr>
<th>Step</th>
<th>Number of targets</th>
<th>Step success rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cloned</td>
<td>107,411</td>
<td></td>
</tr>
<tr>
<td>Expressed</td>
<td>69,381</td>
<td>65%</td>
</tr>
<tr>
<td>Soluble</td>
<td>30,315</td>
<td>44%</td>
</tr>
<tr>
<td>Purified</td>
<td>26,930</td>
<td>89%</td>
</tr>
<tr>
<td>Diffracting crystals</td>
<td>5,082</td>
<td>19%</td>
</tr>
<tr>
<td>Structure determined</td>
<td>3,872</td>
<td>76%</td>
</tr>
</tbody>
</table>

Data from TargetDB
Intasome structure (P. Cherepanov)

retroviral integrase with proviral DNA

Membrane proteins
Protein complexes and assemblies
Flexible multidomain proteins
Glycoproteins
- large amount of protein (10mg)
- pure
- homogeneous
- stable
- concentrated
- diffracting crystals (microcrystals)
- stable in X-ray beam
Integrative structural biology

- X-ray crystallography
- NMR
- cryoEM
- SAXS
- MS
- modeling

Nuclear pore complex architecture (B. Chait, A. Sali, M.P. Rout)
Thank you for your attention