Porada vedoucích

Meeting with Team Leaders



December 5, 2011

Introducing Virology



December 5, 2011



Virology Research-Service Team

Jan Weber 5/12/2011

Outline



- Virology
 - Space
 - Safety
 - Equipment
 - Service plan
 - Research plan
 - Timetable

Space



• BSL2

– one lab with area of 57 m^2

• BSL3

- Two labs with total area of 78 m^2
- Freezer room, centrifugation room
- Three anterooms
- Space for up to 7 people

Safety



- All BSL3 space can be fumigated by
 - Hydrogen peroxide
 - Chlorine dioxide
- Maintained negative pressure in all rooms
- All liquid waste is continuously sterilized
- Solid waste is autoclaved in pass-through autoclave
- Pass-through window with hydrogen peroxide sterilization for material entry/exit
- Personal safety
 - Separate entry and exit anterooms
 - Shower
 - Respiratory protection

Equipment



- BSL3
 - 6 biosafety cabinets (all with outside exhaust)
 - 8 CO₂ incubators
 - Ultracentrifuge Optima max (150 000rpm / 1,000,000g)
 - High performance centrifuge Avanti J-30I (4l, 30,000 rpm / 100,000g)
 - General purpose centrifuge Allegra X-15R (3l, 10,000rpm / 11,000g)
 - Fluorescence microscope (2012)
 - Plate reader for luminescence, fluorescence, absorbance (2012)
 - Bench top flow cytometer (2012)
 - Liquid handling (2013)

Service plan



- General testing of compounds (new, compound archive)
- RNA viruses
 - ssRNA-RT
 - HIV
 - (-)ssRNA
 - Influenza
 - (+)ssRNA
 - Dengue virus
- DNA viruses
 - TBD (from herpes or papilloma family)
- Other viruses

Research plan



- HIV
 - HIV fitness (with University Hospital Na Bulovce)
 - HIV protease (team of Jan Konvalinka and collaborators)
 - Metallacarborane inhibitors
 - Order of processing of Gag and Gag-pol polyproteins
 - New targets for HIV therapy
 - siRNAs (team of Ivan Rosenberg, Dominik Rejman)

Research plan – cont'd



- Dengue virus
 - collaboration with Miguel Quinones at Case
 Western Reserve University, Cleveland, Ohio)
 - Protease inhibitors (team of Pavel Majer)
 - RNA-dependent RNA polymerase inhibitors (team of Zlatko Janeba and Radim Nencka)
- Coxsackie B3 virus
 - Inhibition by carbocyclic nucleoside analogs (team of Helena Mertlíková-Kaiserová)

Timetable



- December 2011 January 2012
 - Complete lab set-up
 - Test all equipment and practices under normal operation (no virus)
 - Hiring 3 people (postdoctoral fellow, university graduate, lab technician)
- February March 2012
 - Start with HIV under normal BSL3 operation
- April June 2012
 - Add influenza, dengue virus
- July August 2012
 - Develop and test screening methods
- September 2012
 - Low volume testing begins
 - Hiring 2 more people (service)

Introducing Medicinal chemistry



December 5, 2011

Research-Service Team of Medicinal Chemistry

Vědecko-servisní skupina medicinální chemie

Head:

Pavel Majer Ph.D.

I would like first to introduce myself Pavel Majer

• 1992

• 1992-1998

- 1998-2006
- 2006-2010

Ph.D. at this institute in the Peptide Chemistry group (Jan Hlavacek, Michal Lebl) in collaboration with Biochemistry group (Peter Strop)

- postdoc, later scientist in the Structural Biology Lab headed by John Erickson at the National Cancer Institute, Frederick, MD, U.S.A.
 - Guilford Pharmaceuticals (later MGI Pharma), Baltimore, MD, U.S.A.
 - Sequoia Pharmaceuticals, Gaithersburg, MD, U.S.A.

My experience

- Originally organic chemist
- Peptide chemistry, solid phase, combinatorial
- Peptidomimetics
- Small molecule drugs
- Structure based drug design
- Design and synthesis of protease inhibitors
- I worked in multidisciplinary teams aimed at developing drugs against HIV, Diabetes, Stroke, Cancer, Hepatitis C etc.
- Focus was always the biological activity of the compounds at the target both in vitro and in vivo





Research

First the service Current Service Staff:

- 6 members of the existing groups were moved under the umbrella of the new team.
- 3 members of the former Service Team of Custom Peptide Synthesis
- 3 members of the former Service Team of Protein Analysis

Services We Provide

- Custom synthesis of peptides
- Custom synthesis of small molecules
- Amino Acid Analysis
- Protein Sequencing
- HPLC Based Assays, Analysis of Amino Acids in Biological Samples

Our Staff



Miroslava Blechová



Alexandrina Prichodko

Custom Synthesis of Peptides

Our Staff



Martin Hradilek Ph.D.

Custom synthesis of small molecules

Our Staff



Zdeněk Vobůrka Věra Himrová Radko Souček

Protein sequencing (Edman)

Amino Acid Analysis (AAA)

AAA and HPLC analysis of derivatized AA

Proposed expansion of service capacity in <u>medium</u> scale custom synthesis

The Goal:

Retaining of some capabilities of the process chemistry group (Pilot Operation), that was recently closed down.

The Situation

- New chemistry facility is currently being built in Papírenská street (10-15 min walk from the institute)
- The construction had been delayed but has resumed lately and should be finished in 2012

The Proposed Plan

- To keep some of the process chemistry medium scale equipment and move it to the "Papírenská" facility
- Hire 2 chemists with some process chemistry experience to man the facility
- Their duties will include small to medium scale custom synthesis of small molecules (targets, intermediates, building blocks) for all research groups of the institute
- Their duties will <u>NOT</u> include synthesis of commercially available reagents, recovery regeneration and distillation of solvents

Now, Last but not Least...the Research Current Research Staff

- Pavel Majer, Ph.D.
- Jitka Bařinková
- ? ... we are in middle of the hiring process...
- ?
- ?
- Students, we just hired Matěj Hájek (UK), Ph.D. Students etc.

The Space

• As of Today None

 As of January ... Lab 204 (SW-wing, second floor) with 3 aisles and 6 Hoods, i.e. Space for about 6 chemists

• To make this lab functional ASAP is currently our main focus

The Mission (impossible)

- We are here to collaborate with everyone
- The more likely primary collaborators are biochemistry groups with interesting targets
- The other collaboration will be with computational groups (the courageous ones, unafraid of the "reality check" of their calculations)
- Help, input, direct involvement in projects etc. from fellow organic chemists will always be welcomed and appreciated

List of current projects

In preparation

- Aurora Kinase (P. Hobza)
- Photo switchable HIV-PR inhibitors (J. Konvalinka)

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In consideration

- Rhomboid inhibitors (K. Strisovsky)
- Antivirals against Yellow Fever (J. Weber)
- And....whatever you suggest.....

Free discussion



December 5, 2011