



Central European Institute of Technology
BRNO | CZECH REPUBLIC

CEITEC: Building Towards Excellence

Czech and Danish Scientists' Workshop on Life Sciences

Markus Dettenhofer

Executive Director

Copenhagen, Denmark 29 April 2014



EUROPEAN UNION
EUROPEAN REGIONAL DEVELOPMENT FUND
INVESTING IN YOUR FUTURE



OP Research and
Development for Innovation

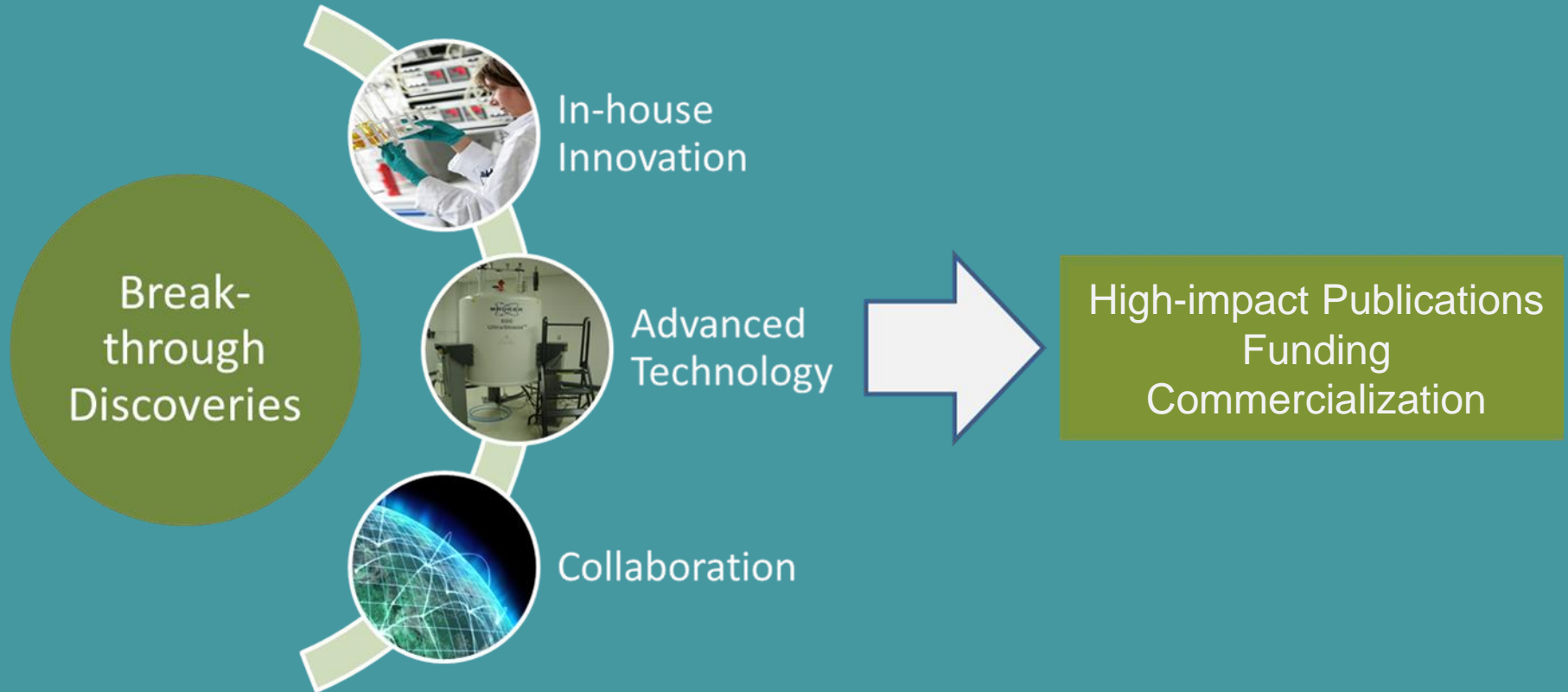


Aim

“ *CEITEC is a scientific centre in the **fields of life sciences, advanced materials and technologies** whose aim is to establish itself as a recognized European center of science.* ”



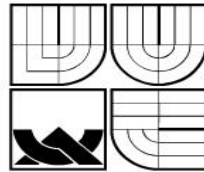
Vision Roadmap



Partnering institutions In Brno, Czech Republic



Masaryk University
www.muni.cz



Brno University of
Technology
www.vutbr.cz



Mendel University
in Brno
www.mendelu.cz



University of Veterinary
and Pharmaceutical
Sciences Brno
www.vfu.cz

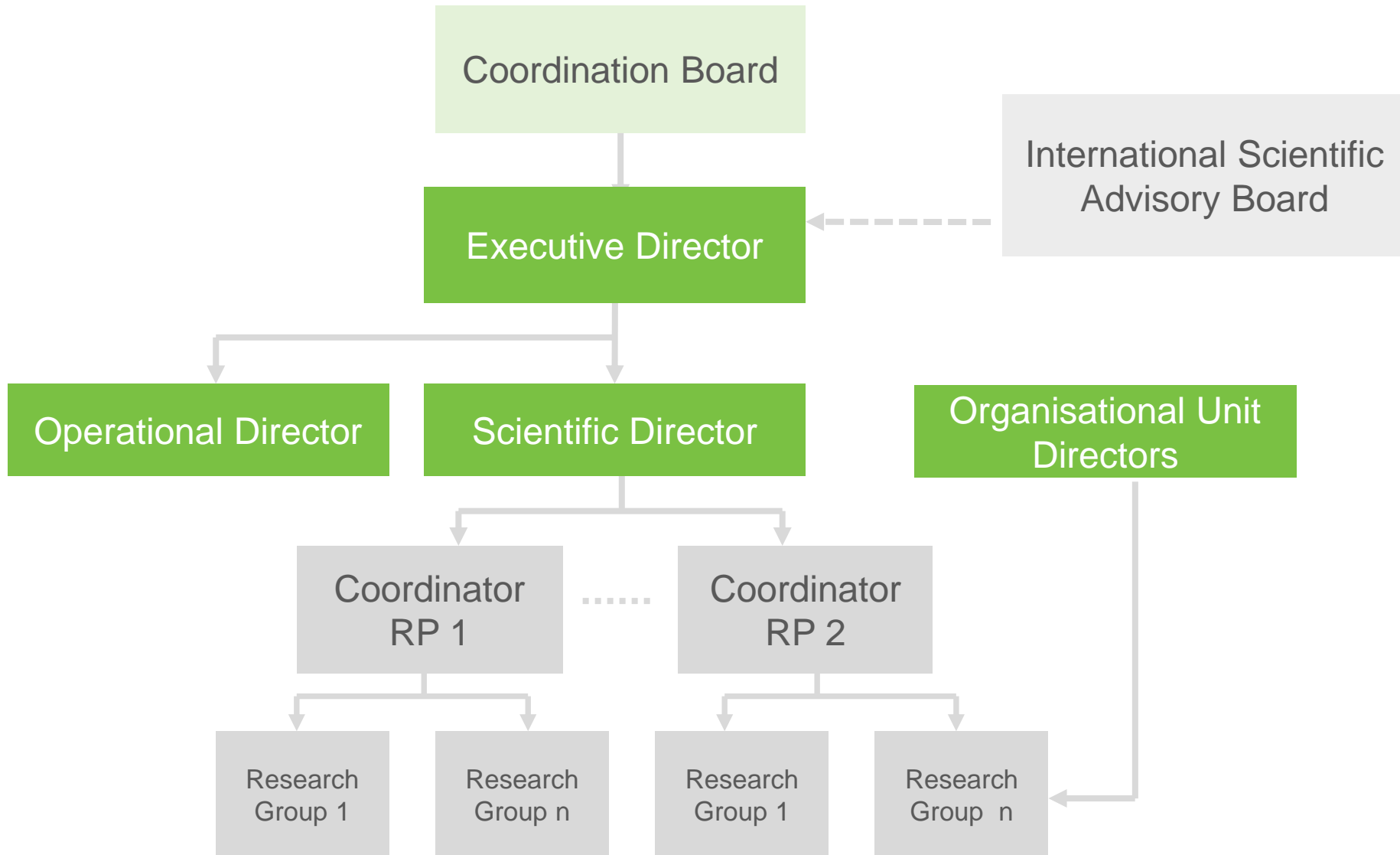


Institute of Physics
of Materials, Academy
of Sciences of the Czech
Republic
www.ipm.cz

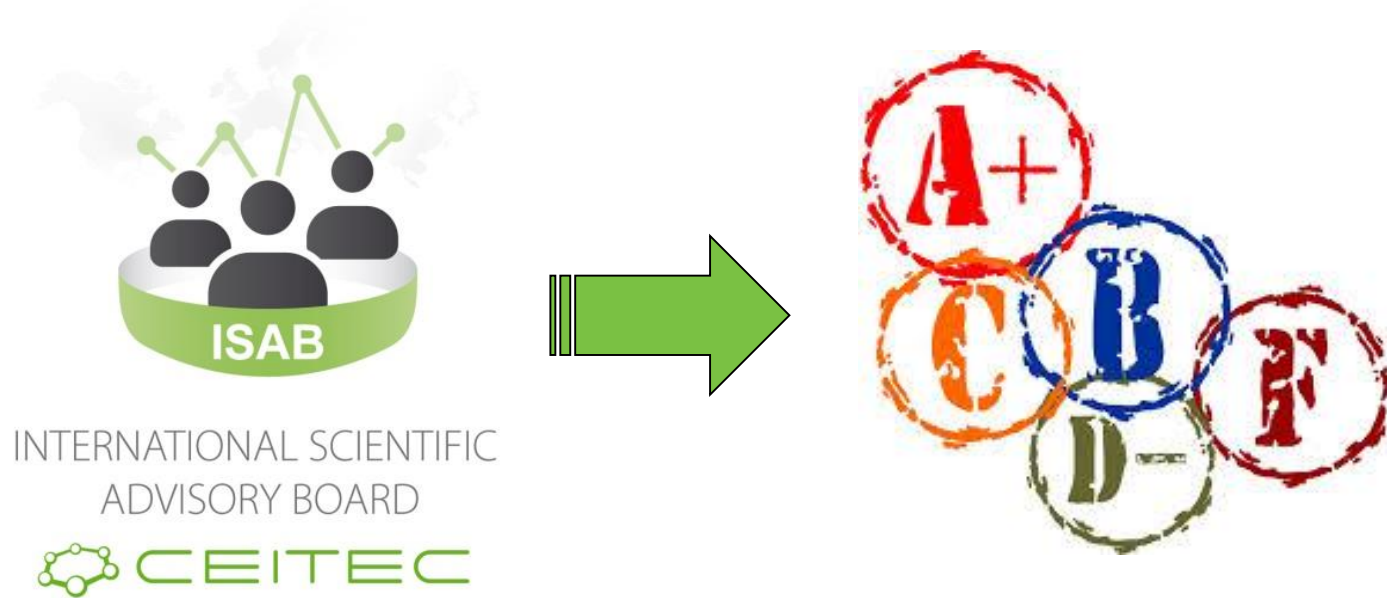


Veterinary Research
Institute
www.vri.cz

Management Structure



Measuring Success Against Global Standards



Board consists solely of Western European and US Members

**Evaluation Sept. 2014 based on past performance, vision plan,
and laboratory visit**

Research Programmes

7. Molecular Veterinary Medicine

6. Brain and Mind Research

5. Molecular Medicine

1. Advanced Nanotechnologies
and Microtechnologies

2. Advanced Materials

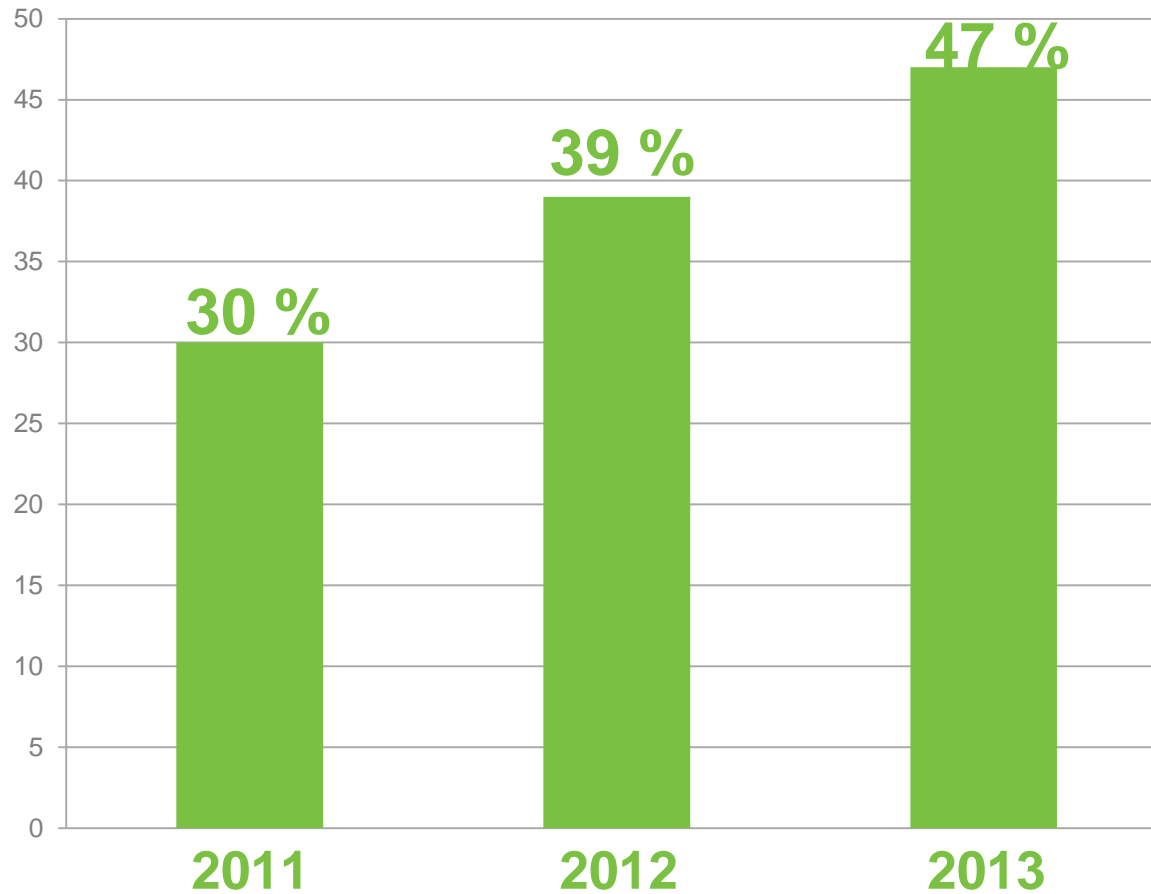
3. Structural Biology

4. Genomics and Proteomics of Plant Systems



61 Group Leaders

CEITEC Publications in Q1%



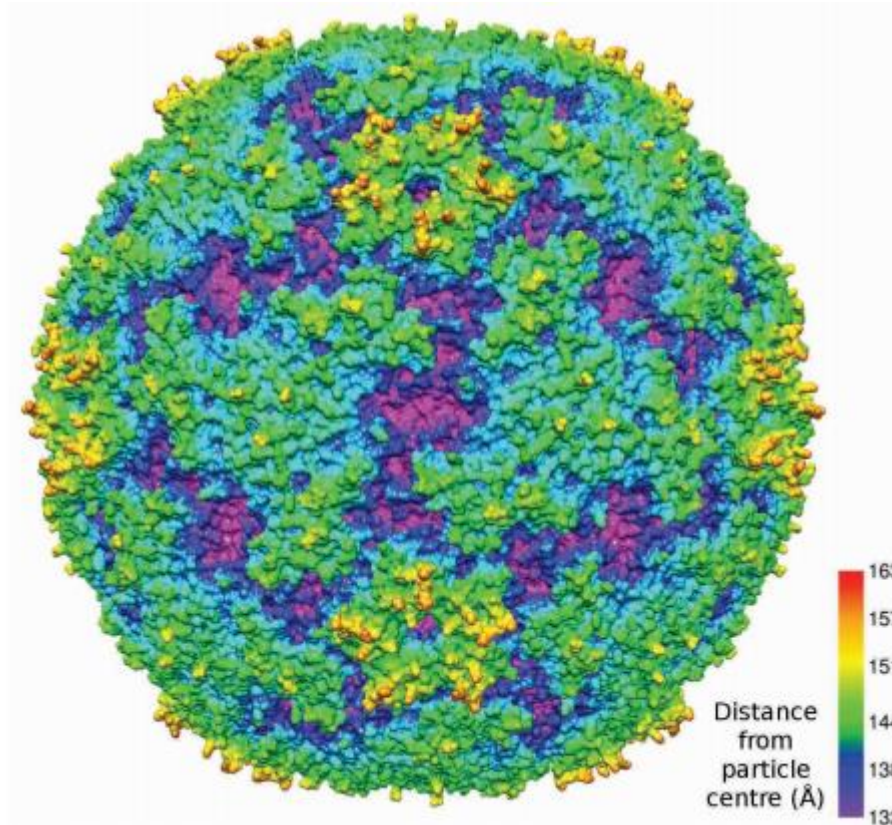
977 CEITEC Publication since start of project

Measures of Excellence

EC definition

- **critical mass** of high level scientists
- **integrating** connected fields
- maintaining a **high rate of exchange** of qualified human resources
- a dynamic role in the surrounding **innovation** system
- high levels of **international visibility** and scientific **connectivity**
- reasonable **stability of funding** and operating conditions over time

CEITEC's First ERC Grant



European Research Council

Established by the European Commission

Molecular surface rendering of EV71
(human enterovirus 71) virus – **Pavel Plevka**

CEITEC's ERA Chair Grant - Recruitment

2,7 M Euro for 5 years.

Purpose: To recruit a **transformational figure** in the area of **Chemical and Cellular Biology**



The future ERA Chair will represent the area of research focusing on exploration of **cellular systems** by advanced imaging methods and their manipulation by means of **small organic molecules and/or state-of-the-art physical methods**.

CEITEC-EU Life strategic partnership



EU-LIFE mission is to foster excellence, share knowledge, and influence research policy in life sciences.



Key Figures (end 2012)
7,039 scientists and support personnel
2,551 publications
59 running coordinated EU-Projects
75 running ERC Grants



RG Plant Cytogenomics (Martin Lysak) – recent publications

Mandáková T, Marhold K, **Lysak MA** (2014) The widespread crucifer species *Cardamine flexuosa* is an allotetraploid with a conserved subgenomic structure. *New Phytologist* 201: 982-992.

Cheng F, **Mandáková T**, Wu J, Xie Q, **Lysak MA**, Wang X (2013) Deciphering the diploid ancestral genome of the mesohexaploid *Brassica rapa*. *Plant Cell* 25: 1541-1554.

Mandáková T, Shimizu Inatsugi R, Zozomová-Lihová J, Shimizu K, Kovařík A, Marhold K, **Lysak MA** (2013) The more the merrier: recent hybridization and polyploidy in *Cardamine*. *Plant Cell* 25: 3280-3295.

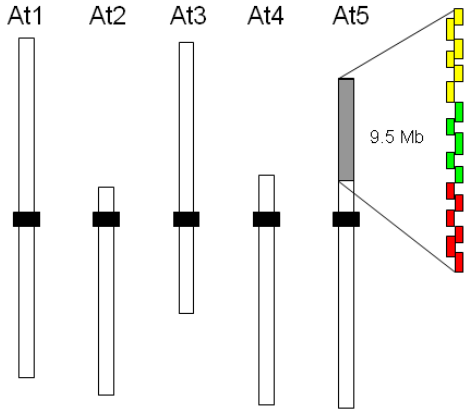
Long Q, Rabanal FA, Meng D, Huber CD, Farlow A, Platzer A, Zhang Q, Vilhjalmsón BJ, **Mandáková T**, **Lysak MA**, Korte A, Nizhynska V, Voronin V, Korte P, Sedman L, Seren U, Hellmann I, Nordborg M (2013) Massive genomic variation and strong selection in *Arabidopsis thaliana* lines from Sweden. *Nature Genetics* 45: 884-890.

Haudry A et al. (2013) An atlas of over 90,000 conserved noncoding sequences provides insight into crucifer regulatory regions. *Nature Genetics* 45: 891-898. [co-authored by Lysak and Mandáková]

Slotte T et al. (2013) The *Capsella rubella* genome and the genomic causes and the genomic consequences of rapid mating system evolution. *Nature Genetics* 45: 831-835. [co-authored by Lysak and Mandáková]

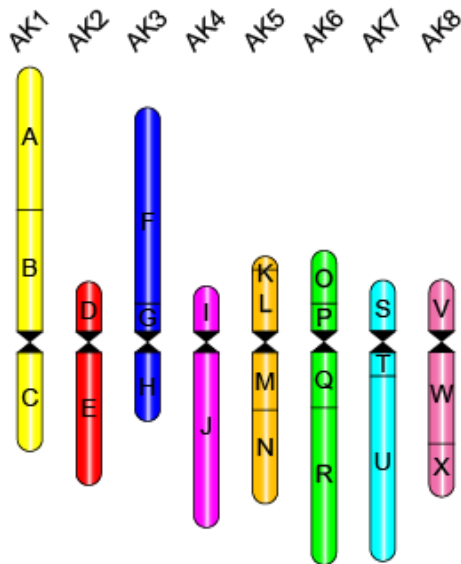
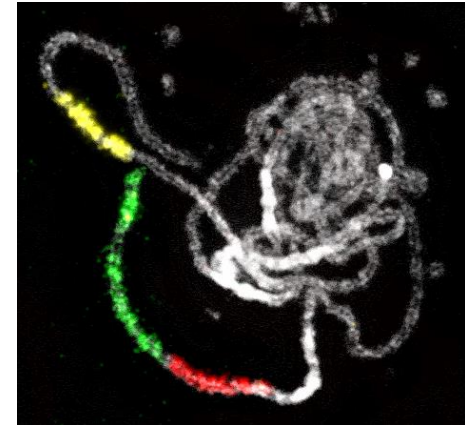
Comparative chromosome painting: principle

Arabidopsis thaliana BACs



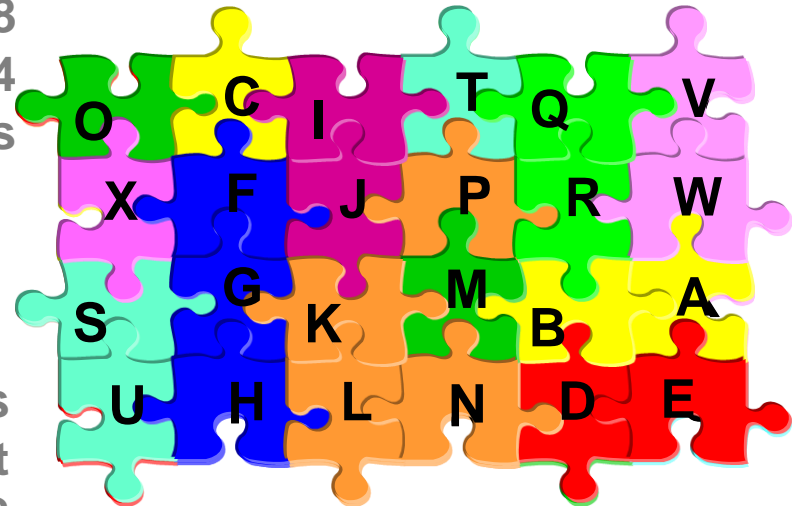
→ BAC contigs →

multicolor fluorescence *in situ* hybridization on meiotic (pachytene) chromosomes



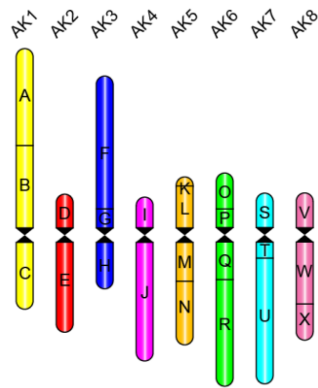
Ancestral Crucifer
Karyotype, 8
chromosomes, 24
genomic blocks

How were the blocks
reshuffled in different
Brassicaceae taxa?

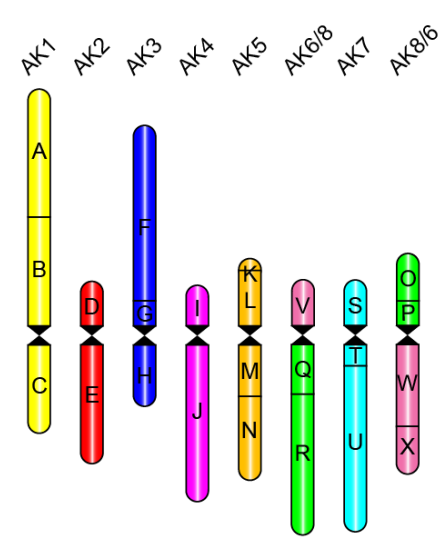


Tribe-Specific Translocation and Karyotype Stasis in the Cardamineae

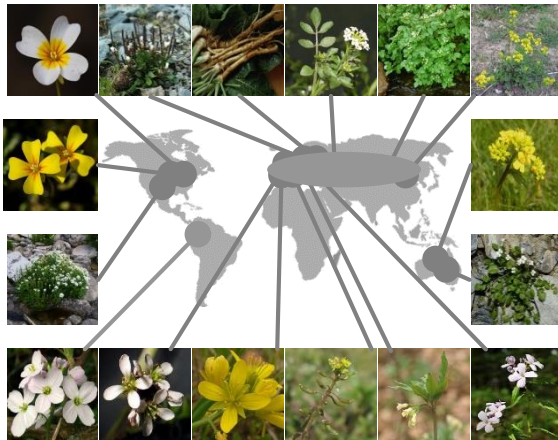
Ancestral Crucifer Karyotype
(n = 8)



Ancestral karyotype of Cardamineae (n = 8)

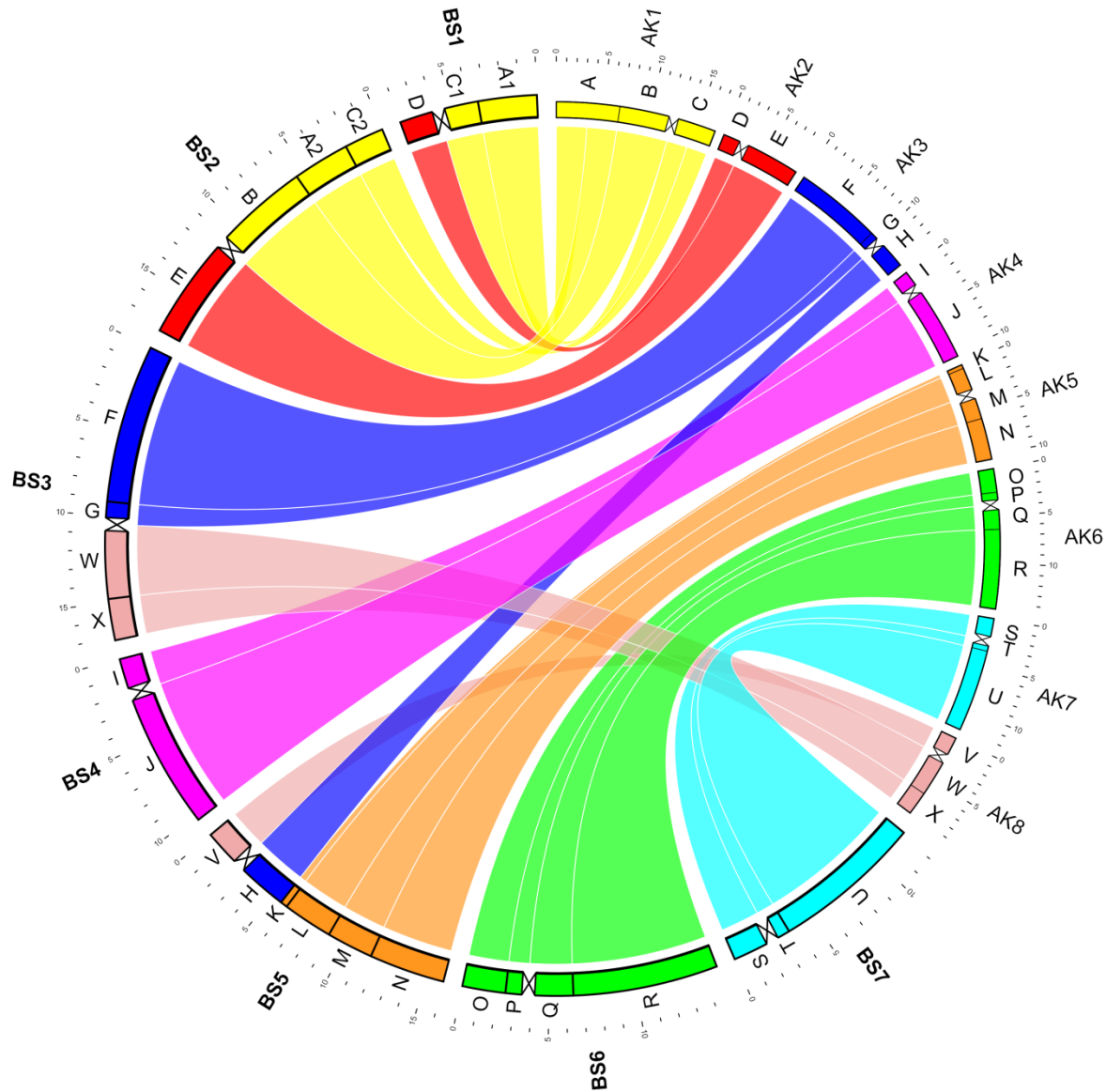


12 genera (337 spp) worldwide

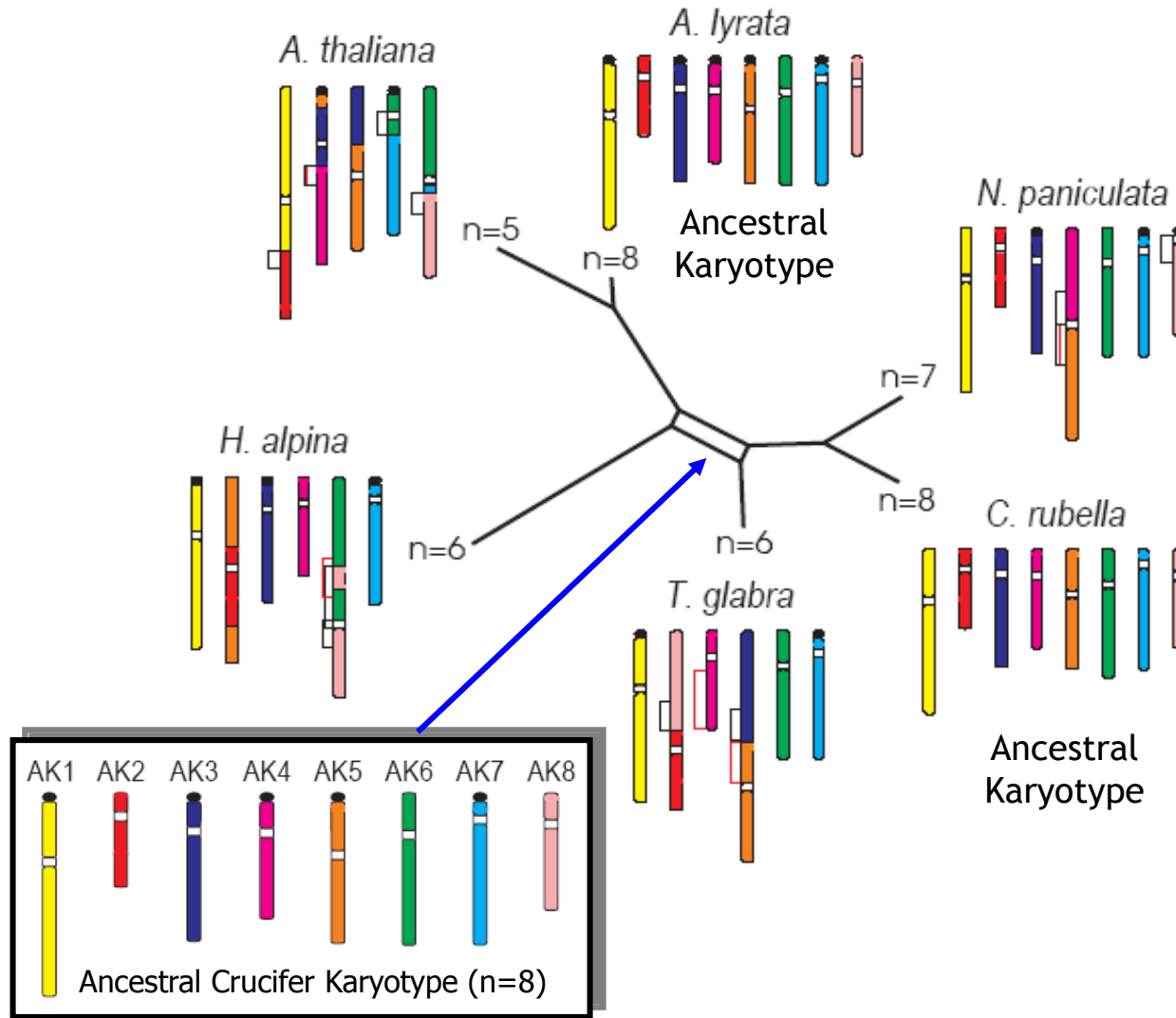


- **Stasis in diploid ($2n = 16$) and autopolyploid ($2n = 32, 48$ or 64) genomes**
- **Genome reshuffling following allopolyploidy (*Leavenworthia*, *Dentaria*)**

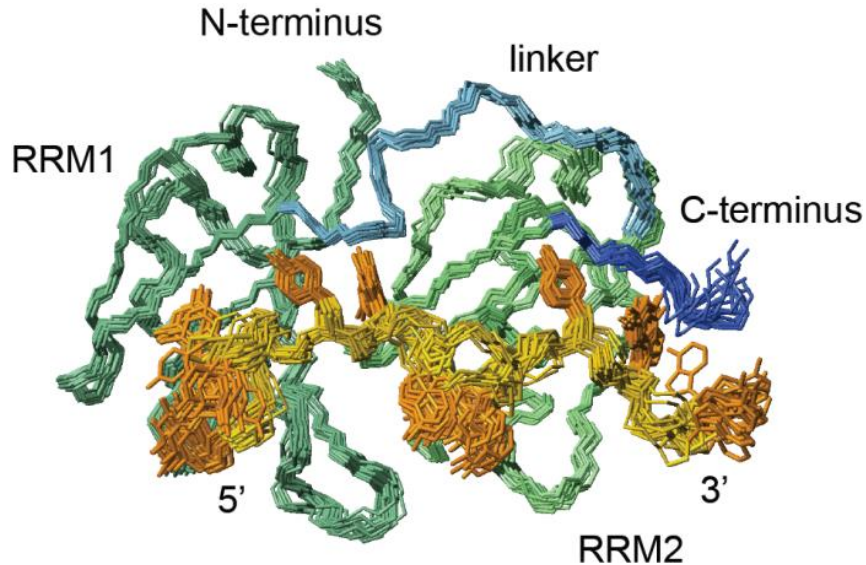
Seven chromosomes of *Boechera stricta* compared with the eight ancestral chromosomes (AK1 - AK8)



Reductions of Chromosome Numbers Were Independent and Used Different Chromosome Breakpoints

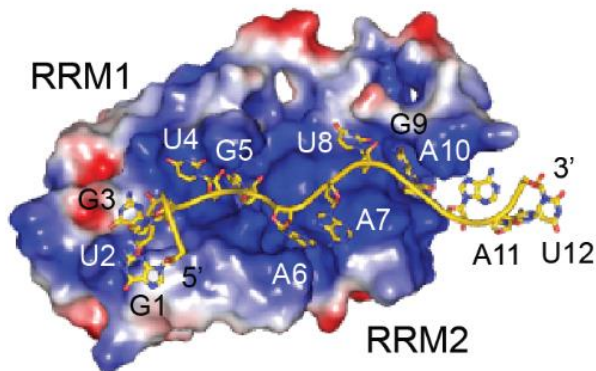


Molecular basis of UG-rich RNA recognition by the human splicing factor TDP-43



Structure of the complex reveals **novel RNA binding mode**

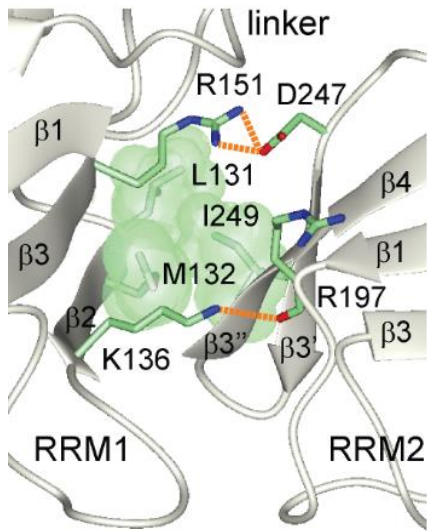
TDP-43 binding to UG-rich RNA associated with **severe forms of cystic fibrosis**



Atomic details of the RNA-protein interactions that lead to **aberrant splicing of an essential exon** in severe forms of cystic fibrosis

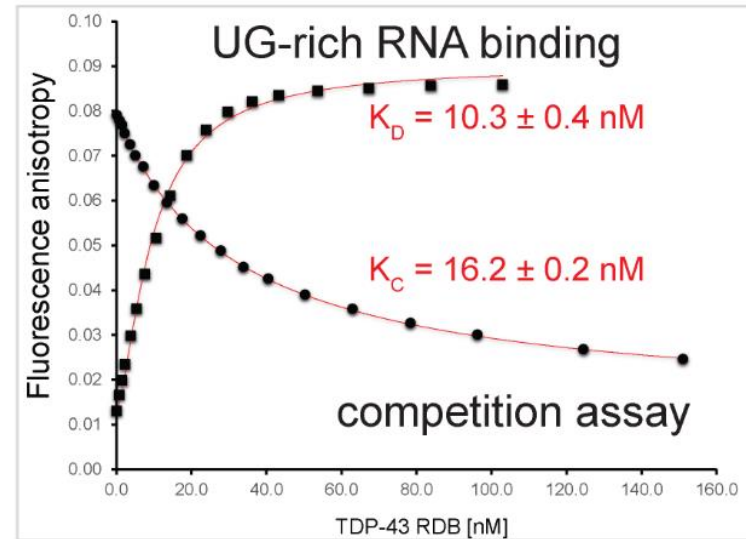
Lukavsky et al., Nature Structural & Molecular Biology 2013

Disrupting TDP-43 – UG-rich RNA interactions restores splicing *in vivo*



Small hydrophobic core
essential for RNA binding

Alanine mutations abolish
RNA binding and **restore**
splicing in cystic fibrosis



Searching for small molecule inhibitors:

Setup of fluorescence-based assay for HTS

Lukavsky et al., Nature Structural & Molecular Biology 2013

Thank you for your attention



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