

1) Model plant *Arabidopsis thaliana*

Update 2013

Harter K, Weber APM (2013) Arabidopsis 2010 and beyond – big science with a small weed.
Frontiers in Plant Science 4: 1

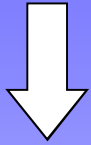
Rhee SY, Mutwil M (2013) Towards revealing the functions of all genes in plants.
Trends in Plant Science 19: 212-221

Martin Fellner
Laboratory of Growth Regulators
Faculty of Science, Palacky University in Olomouc
and Institute of Experimental Botany
Czech Academy of Science

1) Plants are essential for life on Earth



Necessity of plants for human existence on the Earth



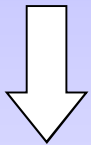
Need to streamline agriculture in order to feed Earth population



Need to learn essentials of molecular and physiological processes in plants = to learn about gene function



Study of the most simple organisms = faster discovery of gene functions



Model plants needed

2) What is *Arabidopsis* and why is so attractive as a model plant?



- a) Produces thousands of seeds on one plant
- b) It has fast life cycle: 6-8 weeks
- c) It is autogamous (self-fertile) and diploid
- d) It is a short plant: 10 – 30 cm
- e) Easy to be mutated and transformed
- f) It has low number of chromosomes and small genome

1907 Friedrich Laibach, Bonn, Germany – first who worked on *Arabidopsis thaliana*: **5 chromosomes**

1943 proposed *Arabidopsis* as a **model plant**

a) Produces thousands of seeds on one plant

High number of seeds is optimum for mutagenesis -
- it is possible to mutate high number of seeds at the same moment => bigger chance of successful mutagenesis.

High number of seeds is convenient for study of mutations and for genetic tests.

b) It has fast life cycle: 6-8 weeks

Arabidopsis grows for full year and it has several generations. Short life cycle allows fast genetic analysis.

c) It is autogamous (self-fertile) and diploid

Flowers do not produce nectar => little attractive for insect =>
=> plants developed the autogamy => they are homozygous lines.

Thanks to the diploidy recessive characters can be easily identified.



d) It is a short plant: 10 – 30 cm

Economic cultivation of plants: thanks to short stature we can cultivate a large number of plants on the small area in a greenhouse or in growth chambers.

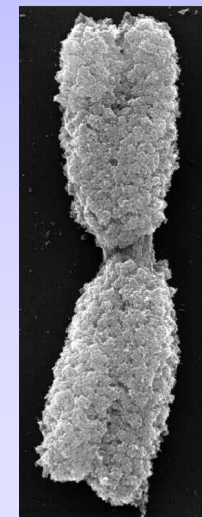
e) Easy to be mutated and transformed

Thanks to a large number of mutants and transformed plants, the identification of genes, gene cloning and study of their function is faster.

f) It has low number of chromosomes and small genome

Arabidopsis has 5 chromosomes; DNA is formed by $100-120 \times 10^6$ bp (base pairs).

Small genome results from small amount of repetitive DNA: 90% nuclear DNA codes for proteins => fast saturation of the genome by mutations and fast identification of genes.



5x

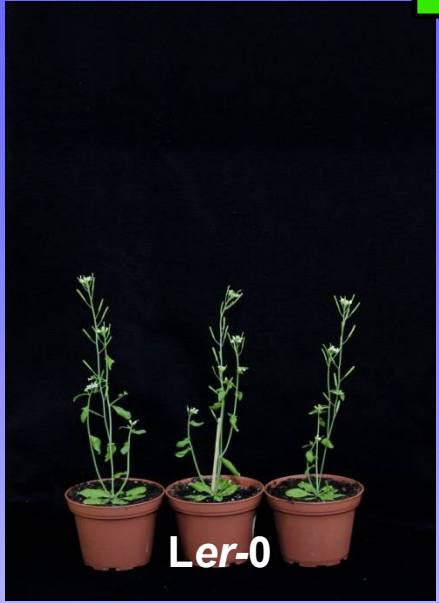


Photo: Hana Martinková (LGR)



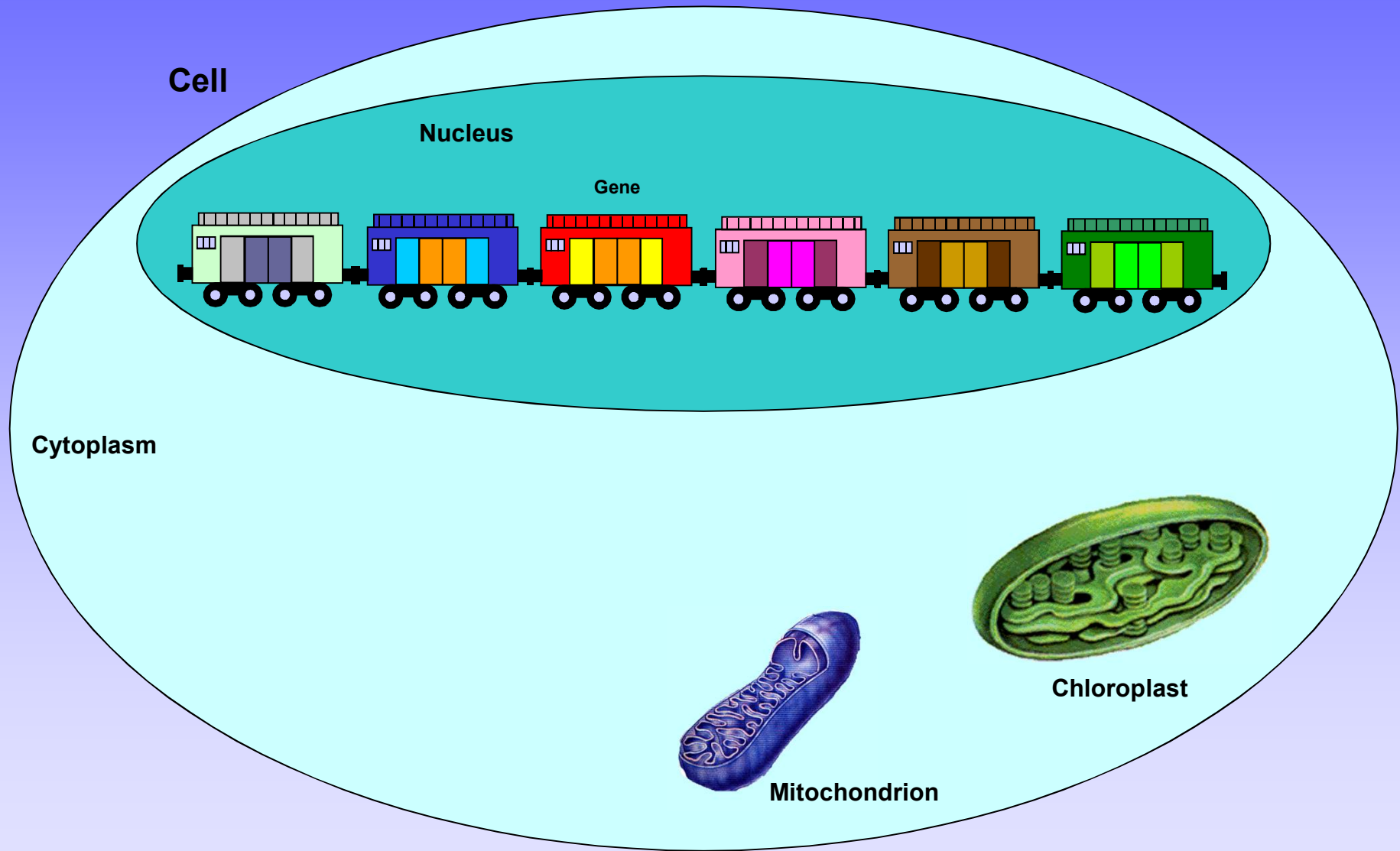
PMP



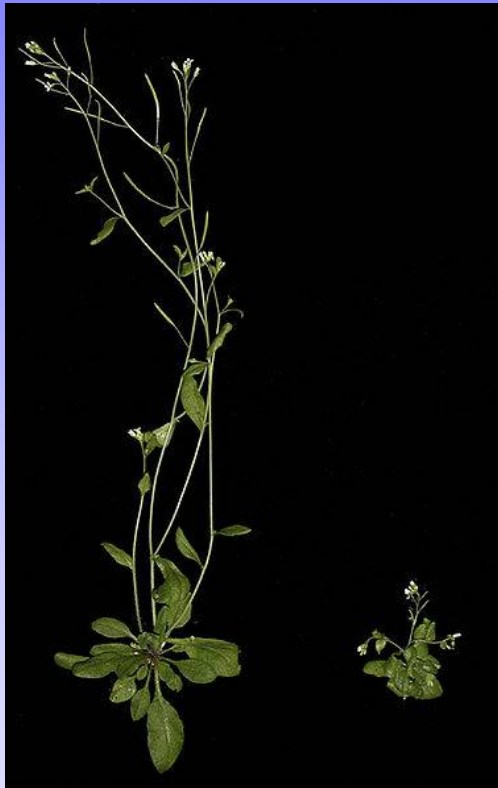
**Photo:
Hana Martinková
(LGR)**



Gene, DNA sequence DNA, protein, genome

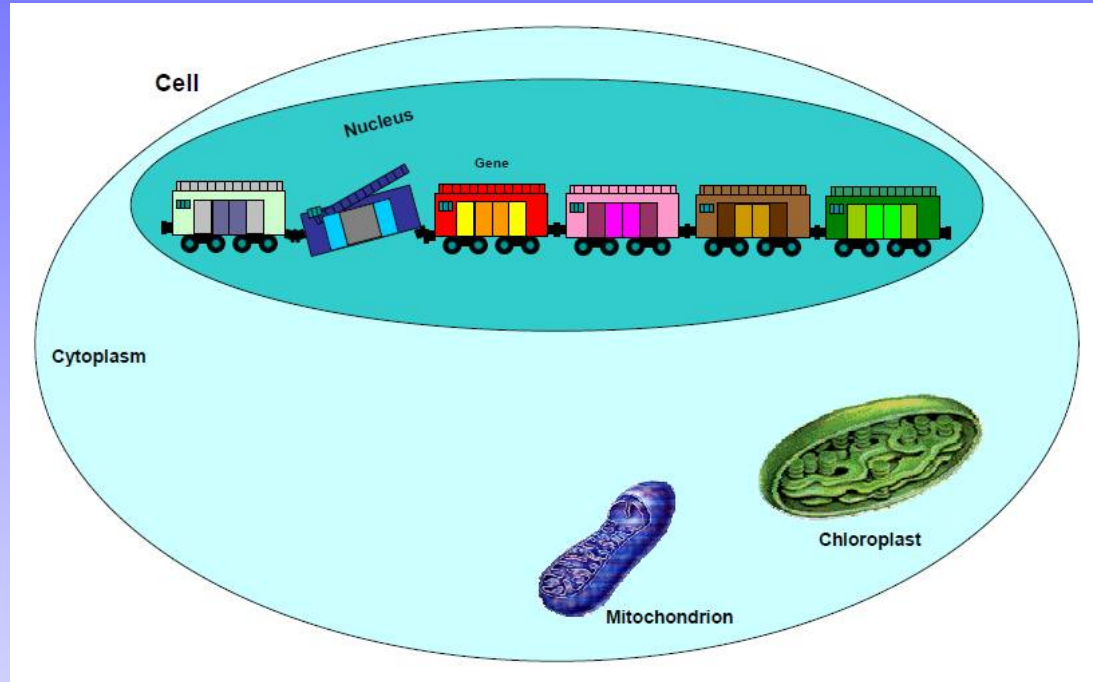


Mutant = an organism with a change in DNA sequence



Unmutated (normal) plant (wild-type)

Mutated plant



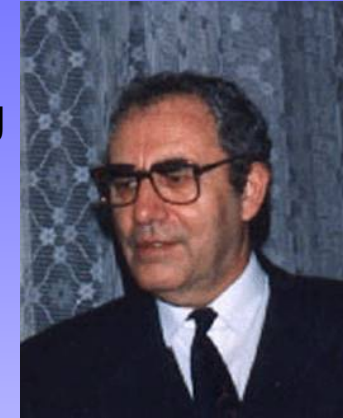
Mutated gene is involved in elongation in some way.

3) Development of *Arabidopsis* community.

XIth Genetic congress in Haag (1963)

Established *Arabidopsis* information service (AIS) – sharing Information about *Arabidopsis*

First AIS Newsletter was published – Czech scientist **Jiří Velemínský.**



1965 – 1st *Arabidopsis* symposium in Göttingen, Germany, 25 participants.

Physiological and genetic study of mutants, 1st report about genetic mapping and mutagenesis methods

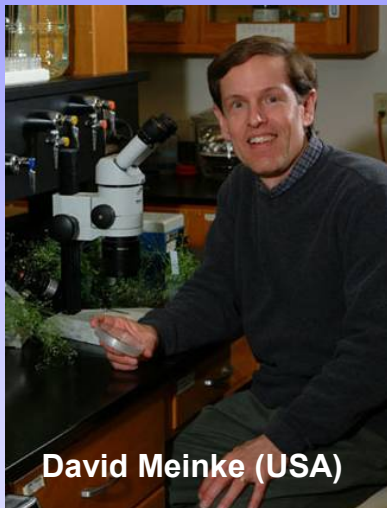
70th – The interest in *Arabidopsis* declines

Scientists are interested in economically important plants – greater chance to receive funds for research.

70th: only some groups of scientists continue in *Arabidopsis* research:

- Jaap van der Veen (Netherlands) - mutagenesis, flowering, hormones
- Paddy Maher (UK) - auxin-sensitive mutants
- WJ Feenstra (Netherlands) – mutants in nitrogen transport
- David Meinke a Yan Sussex (USA, Oklahoma) – embryo-lethal mutants

<http://www2.okstate.edu/pio/12.13.00genome.html>



David Meinke (USA)

These groups generated and selected a number of mutants and distinguished real importance of *Arabidopsis* as a model plant.

1983 –1st genetic map of *Arabidopsis thaliana* published by Prof. Marteen Koornneef (Netherlands, Wageningen)



Interest in *Arabidopsis*



Marteen Koornneef (Holandsko)

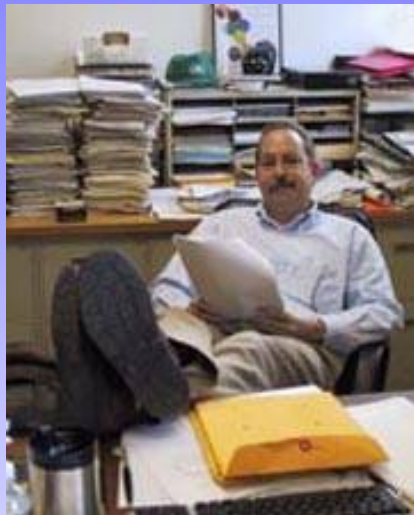
http://www.gen.wur.nl/UK/Staff/Scientific+Staff/Maarten+Koornneef/?wbc_purpose=Basic&WBCMODE=PresentationUnpublished

4) Molecular era

Birth of molecular biology at the beginning of 80th – a promise of new epoch-making discoveries in plant biology (+ George Rédei).



George Rédei (USA)



Elliot Meyerowitz (USA)

<http://www.its.caltech.edu/~plantlab/>



Fred Ausubel (USA)

<http://ausubellab.mgh.harvard.edu/>

Basic discoveries to turn of 70th and 80th:

- Ability of *Agrobacterium tumefaciens* to transfer its DNA into nuclear genome of higher plants => turn in possibilities to investigate gene functions
- Confirmation of size of *Arabidopsis* nuclear genome = **70 x 10⁶ bp** => faster gene cloning

Famous scientists, working in different fields of biology understood the importance of small *Arabidopsis* genome for fast cloning and identification of genes:

- Ron Davis – investigation of yeasts
- Gerry Fink - investigation of yeasts
- Howard Goodman – founder of molecular biology

End of 80th – adoption of *Arabidopsis*



Gerry Fink (USA)



1987 Elliot Meyerowitz – a vision of investigation of *Arabidopsis* genome – gene cloning using positional cloning; research strategy

Meyerowitz EM (1987) *Arabidopsis thaliana*. Annu Rev Genet 21: 93-111

Meyerowitz and Goodman established genomic sources (RFLP maps, YAC libraries, etc.), which makes gene cloning easier and faster.



1992 First genes were cloned using positional cloning – the work lasted **2 years**

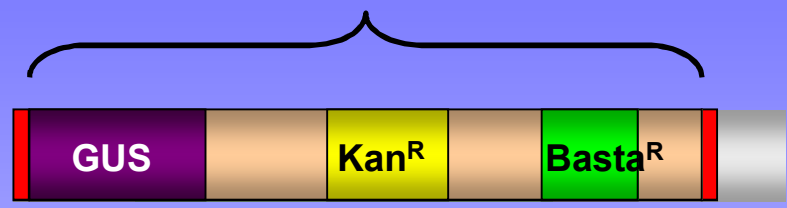
1987 Ken Feldman and David Marks – first collection of T-DNA mutants in *Arabidopsis*

David Marks (USA)

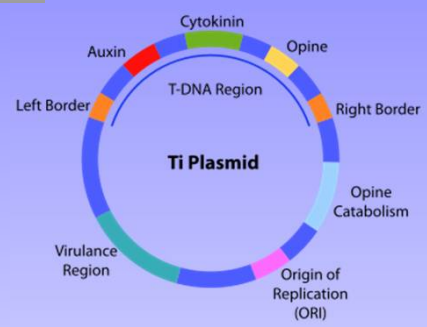


<http://www.cbs.umn.edu/node/1864>

T-DNA construct introduced into plant DNA by means of *Agrobacterium tumefaciens*



Unknown gene, which we wish to clone (= to find its sequence)

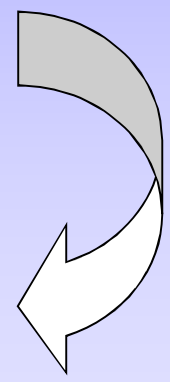


1989 First gene from this collection was cloned during **several months**

Marks D, Feldman K (1989) *Plant Cell* 1: 1043-1050
 Feldman K et al. (1989) *Science* 243: 1351-1354

<http://www.plantcell.org/cgi/content/full/1/11/1043>

New era of molecular biology in *Arabidopsis*





End of **80th** is typical by growing interest in *Arabidopsis*



Conference on *Arabidopsis* in Michigan 1987: 217 participants



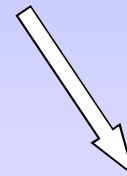
1988 Formation of first electronic group = Information *Arabidopsis* Service;
today substituted by databases

TAIR a GARNET



The Arabidopsis Information Resource

<http://www.arabidopsis.org>



Genomic Arabidopsis Resource Network

<http://www.garnetcommunity.org.uk/>

Fast improvement of transformation methods *Arabidopsis* => more efficient transformation methods => fast saturation of *Arabidopsis* genome

1993 George Pelletier, INRA, France – transformation of *Arabidopsis* methods *in planta* => large T-DNA mutant collections

<http://weedsworld.arabidopsis.org.uk/Vol2ii/pelletier.html>

Example of use of T-DNA mutants: selection of mutants, whose analysis resulted in identification and cloning of homeotic flower genes *AG*, *PI*, *AP2*, *AP3*.



Laboratory of E. Meyerowitz:
elegant model of development
of flower genes:

ABC model



Marteen Koornneef (Holandsko)



Bowman JL et al. (1991) *Development* 112: 1-20

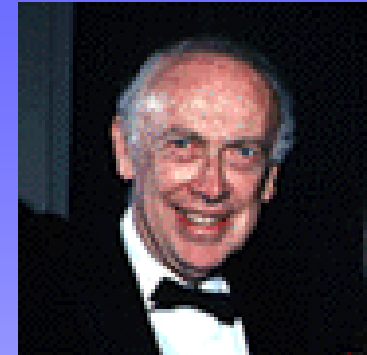
John Bowman (USA)



<http://www.biolsci.monash.edu.au/staff/bowman/index.html>

5) *Arabidopsis* projects

1989 James Watson (Cold Spring Harbor Laboratory; co-discoverer of DNA, Nobel Prize 1962) – initiated discussion meeting about *Arabidopsis* (Eric Bloch – NSF).



James Watson (USA)

Ron Davis
Gerry Fink
Elliot Meyerowitz
Chris Somerville
Ken Feldman

<http://www.cshl.edu/gradschool/Non-Research-Faculty/james-d-watson>

Strategy of the **1th *Arabidopsis* project**, shielded by Watson and supported by National Science Foundation (NSF)



Chris Somerville (USA)

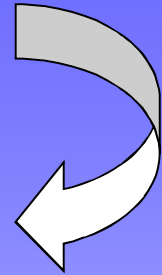
1990 Formation of National and Multinational *Arabidopsis* Steering Committees – call for laboratories around the world for work on *Arabidopsis*.

Aim of the project: To sequence the whole *Arabidopsis* genome by 2003.

<http://epmb.berkeley.edu/facPage/dispFP.php?l=1417>

Need to create an infrastructure to organize and to share information between laboratories.

1991 Creation of *Arabidopsis* Stock Center in USA and UK, development of databases, libraries of clones, mapping polymorphism, etc.



USA – more focused on development of infrastructure and genomic sources

Europe – more focused on particular sequencing - **BRIDGE project** = collaboration of 33 laboratories in 9 countries

- **UK** - separate project = connection of 41 laboratories in 9 countries

1993 - ESSA project = 19 laboratories – focused on sequencing of continuous 2500 kb regions on chromosomes III, IV and V.

1993 – Established Kazusa DNA Research Institute in Japan = involvement of Japan to sequencing of *Arabidopsis* genome.

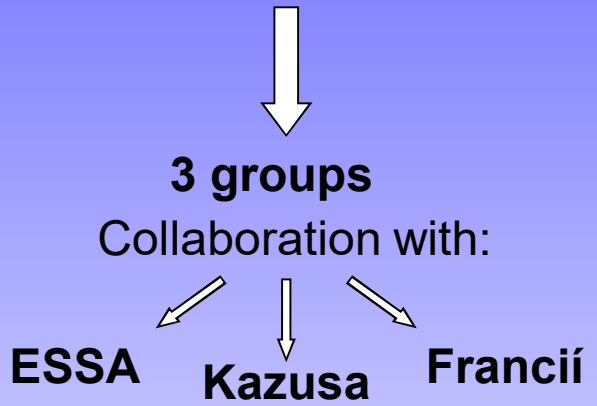
Rob Martiessen
Dick McCombie
Joe Ecker

} **USA project** – involvement into sequencing; supported by NSF and USDA



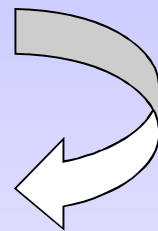
Joe Ecker (USA)

<http://www-biology.ucsd.edu/faculty/ecker.html>



1996 Mechanism of coordination and cooperation settled

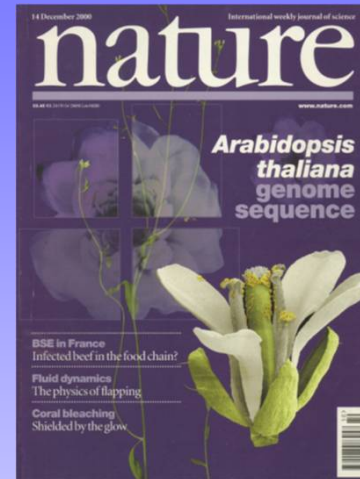
Formation of ***Arabidopsis* Genome Initiative**



2000 Sequencing of *Arabidopsis* genome terminated

Published in special issue of Nature:

Nature 408: 796 – 826, 2000



Analysis of the genome sequence of the flowering plant *Arabidopsis thaliana* THE ARABIDOPSIS GENOME INITIATIVE

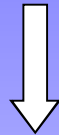
Authorship of this paper should be cited as "*The Arabidopsis Initiative*"

The Institute for Genomic Research, 9712 Medical Centre Drive, Rockville, Maryland 20850, USA
Kazusa DNA Research Institute, 1532-3 Yana, Kisarazu, Chiba 292, Japan

The flowering plant *Arabidopsis thaliana* is an important model system for identifying genes and determining their functions. Here we report the analysis of the genomic sequence of *Arabidopsis*. The sequenced regions cover 115.4 megabases of the 125-megabase genome and extend into centromeric regions. The evolution of *Arabidopsis* involved a whole-genome duplication, followed by subsequent gene loss and extensive local gene duplications, giving rise to a dynamic genome enriched by lateral gene transfer from a cyanobacterial-like ancestor of the plastid. The genome contains 25,498 genes encoding proteins from 11,000 families, similar to the functional diversity of *Drosophila* and *Caenorhabditis elegans*— the other sequenced multicellular eukaryotes. *Arabidopsis* has many families of new proteins but also lacks several common protein families, indicating that the sets of common proteins have undergone differential expansion and contraction in the three multicellular eukaryotes. This is the first complete genome sequence of a plant and provides the foundations for more comprehensive comparison of conserved processes in all eukaryotes, identifying a wide range of plant-specific gene functions and establishing rapid systematic ways to identify genes for crop improvement.

6) Functional Genomics Project

In 1988, before completion of the sequencing project, Joe Ecker initiated a workshop.



He proposed a new project.



Joe Ecker (USA)

Project mission: To determine function of all *Arabidopsis* genes



Joe Ecker
Joan Chory
Detlev Weigel



In 2000, the project was developed and published in *Science*:

Science, Vol 290, Issue 5499, 2077-2078,
15 December 2000

<http://www.sciencemag.org/cgi/content/full/290/5499/2077>

Joan Chory (USA)

<http://www.salk.edu/faculty/chory.html>

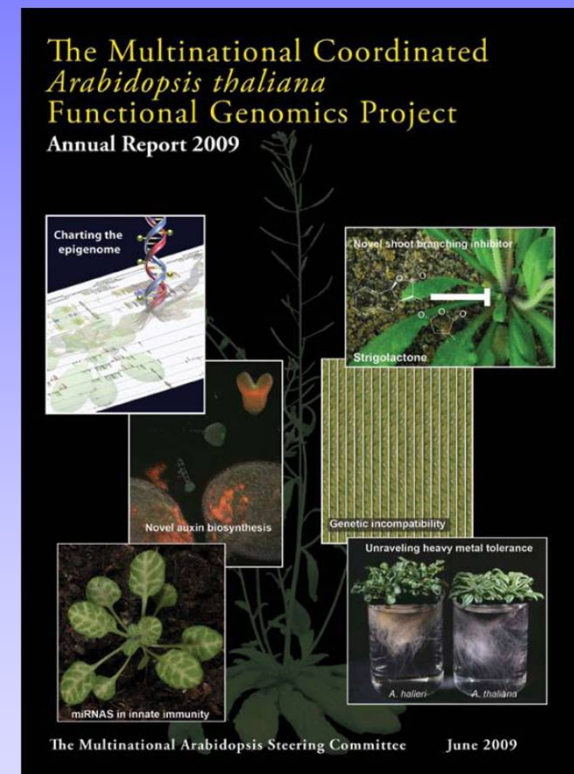


Functional Genomics Project: 2001 - 2010

Aim of the project:

http://www.arabidopsis.org/portals/masc/2009_MASC_Report.pdf

- 1) To develop genetic tools, including new technologies of the development, which allow general scientific public to perform functional genomic research on *Arabidopsis*.
- 2) To identify function of genes of whole system: gene expression, protein analysis, dynamics of metabolites, molecular interaction, comparative genomics.
- 3) To expand role of bioinformatics
- 4) To develop community and human resources
- 5) Improvement of international collaboration



Regular annual reports MASC (The Multinational *Arabidopsis* Steering Committee): **2002, 2003,** => <http://www.arabidopsis.org> => Functional Genomics => <http://www.arabidopsis.org/portals/masc/index.jsp>

Functional Genomics Project: 2001 - 2010

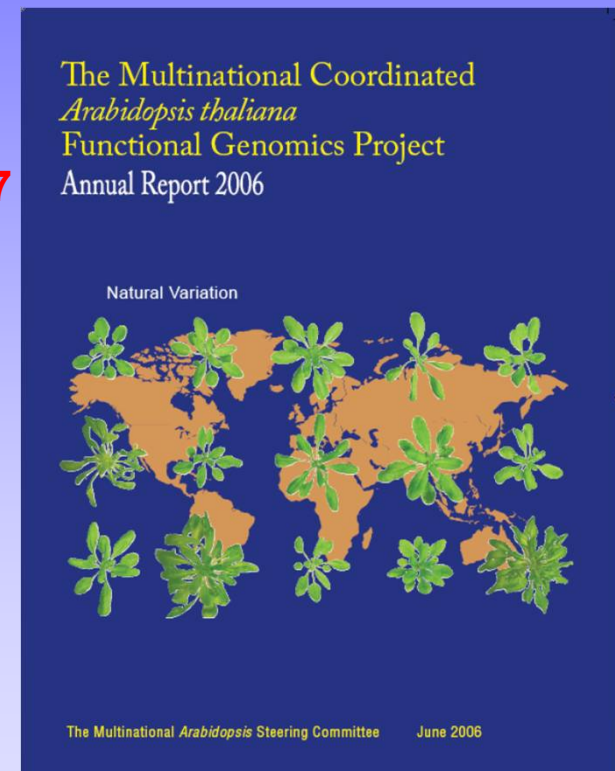
<http://www.nsf.gov/pubs/2002/bio0202/2010report.pdf>

Main results during last 5 years:

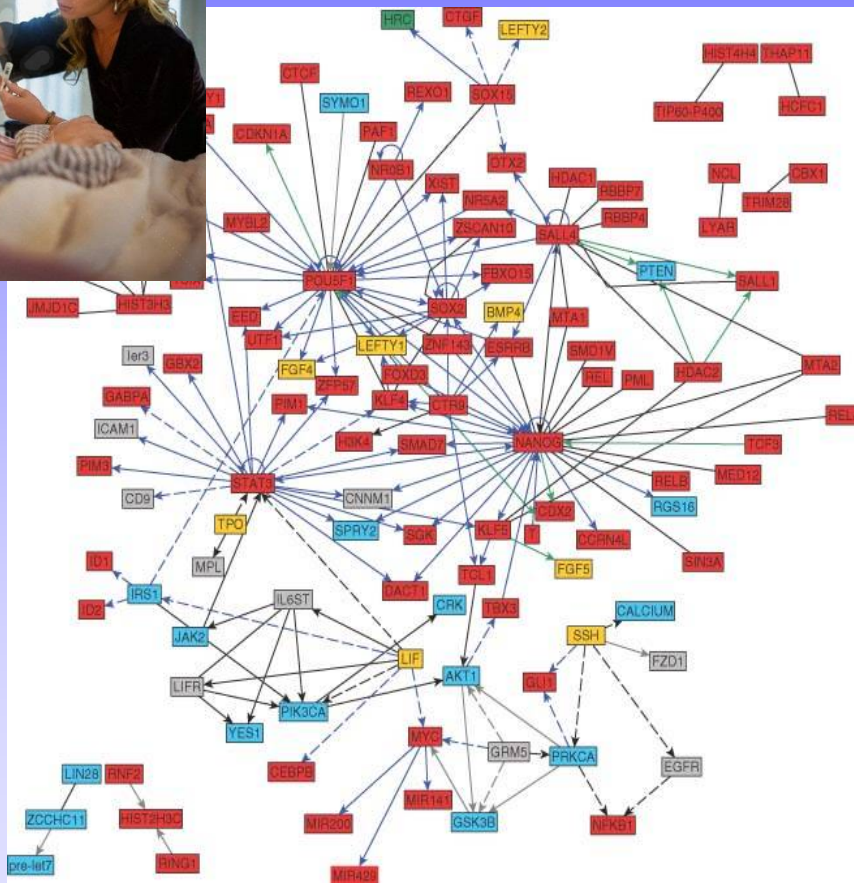
(Bevan and Walsch 2006, Genome Research 15: 1632-1642)

- 1) Specification of *Arabidopsis* genome size: **146 Mbp**
- 2) Prediction of number of protein coding genes: **26 207**
- 3) Number of protein coding genes, of which transcripts were identified : **19 117**
- 4) Number of proteins: **27 855**
- 5) Number of genes with the inserts in exon and intron region: **24 589**

Current main objective: use of project results for identification of developmental relations among plants, specifically crops



7) Arabidopsis and human diseases



Human being is not a good experimental object



Model organisms:

Saccharomyces cerevisiae

Drosophila melanogaster

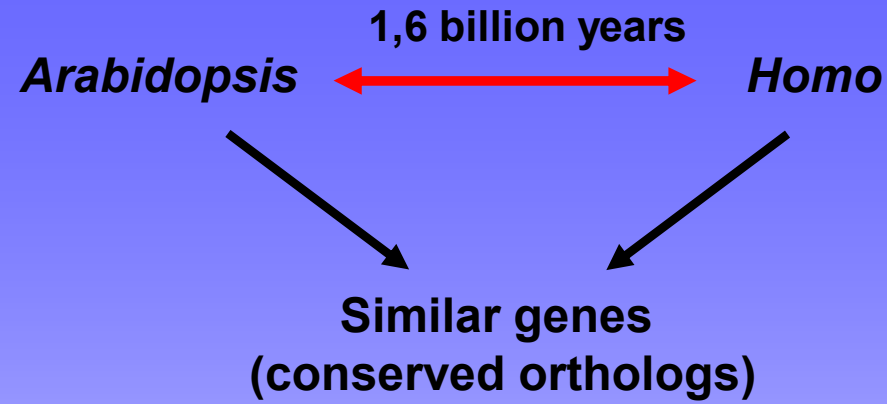
Caenorhabditis elegans

+

Arabidopsis thaliana



Comparison of human genome with genomes of model organisms



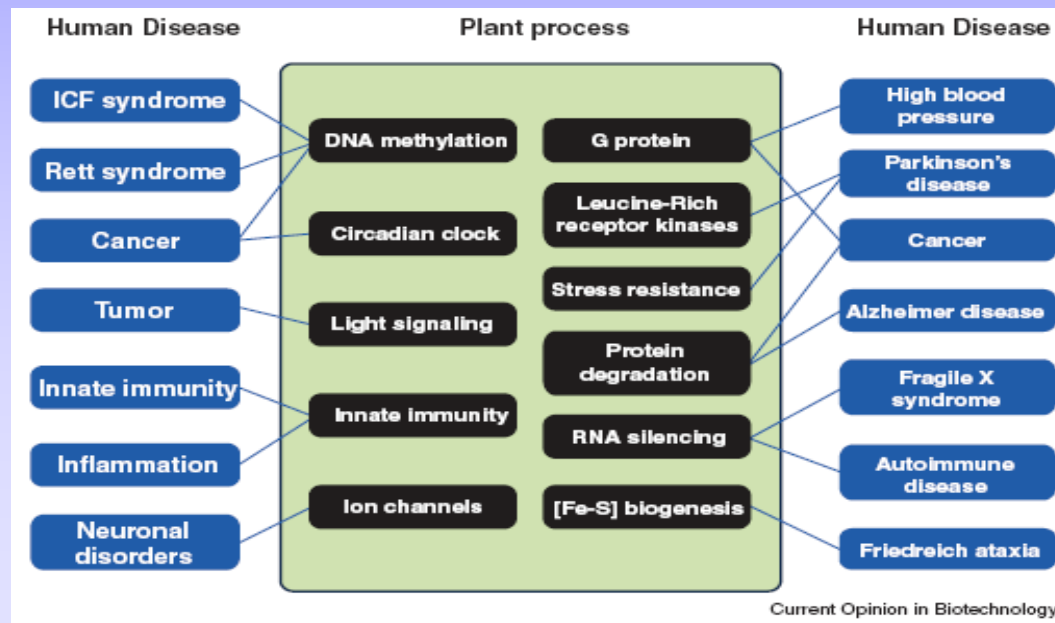
Orthologs: Neurological disorders:
Cancers:

71% genes (*Arabidopsis*)

70% genes (*Arabidopsis*)

67% genes (*Drosophila*)

41% genes (*Saccharomyces*)



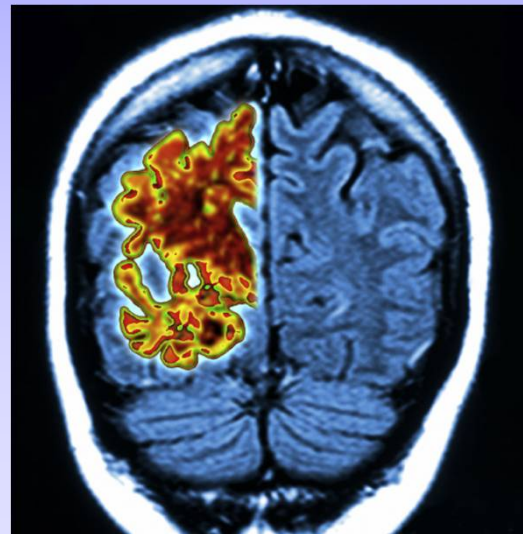
Xu XM, Møller SG (2011) Current Opinion in Biotechnology 22: 300–307

Significance of *Arabidopsis* in the study of molecular mechanisms of Alzheimer's disease

- Alzheimer's disease – most common age-related neurodegenerative disorder
- Deposition of small proteins β amyloids ($A\beta$) \longrightarrow degeneration of neurons



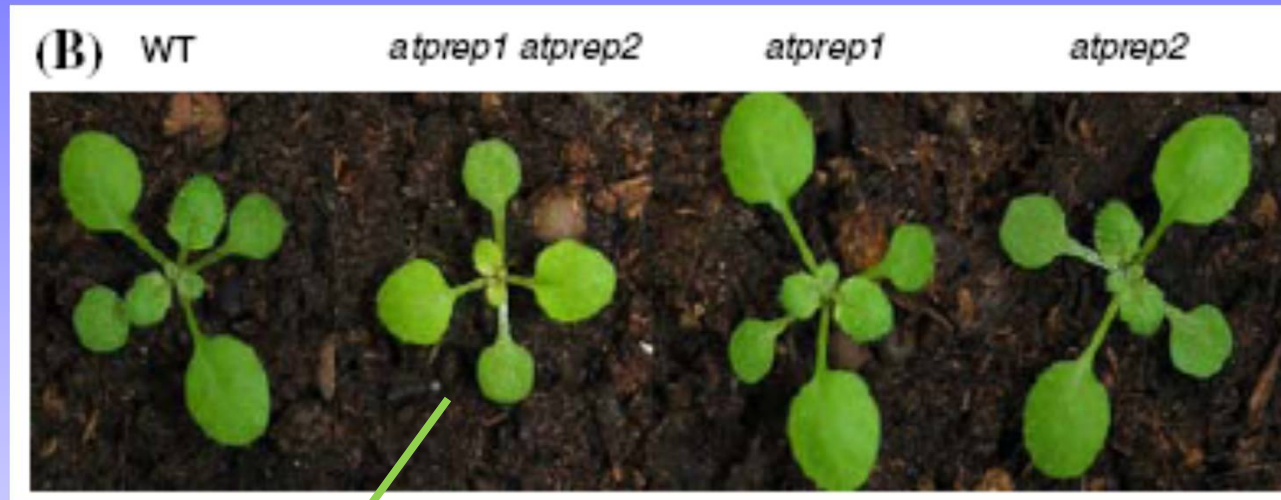
APP – **A**myloid **P**recursor **P**rotein;
expressed in neurons, function
unknown



Neurological disease gene orthologs found in *Arabidopsis*

Human disease genes	Arabidopsis ortholog	E-values	Function in <i>Arabidopsis</i>
Adrenoleukodystrophy-ABCD1	At4g39850	9.6e-86	Peroxisomal ATP binding cassette protein (PXA1)
Alzheimer-APP	At5g59390	8.7e-03	XH/XS domain-containing protein AXR1-like
Alzheimer-APP-BP1	At1g05180	1.2e-113	Auxin-resistant 1 (AXR1)
	At2g32410	2.3e-114	AXR1-like (AXL)
Alzheimer-PSEN1	At2g29900	1.7e-36	Presenilin family protein
Alzheimer-PSEN2	At1g08700	9.2e-36	Presenilin family protein
Alzheimer-APOE	At2g38370	1.4e-03	Unknown protein
Alzheimer-CLU	At3g15550	3.1e-01	Unknown protein
Alzheimer-PICALM	At2g01600 ⁺	4.3e-25	ENTH domain-containing protein
Alzheimer-PreP-PITRM1	At3g19170	6.1e-118	AtPreP1 (Pre-sequence protease)
	At1g49630	2.7e-115	AtPreP2
Amyotrophic Lat Sclero-SOD1	At2g28190 ⁺	2.8e-45	Cu/Zn superoxide dismutase-like protein (CSD2)
Angelman-UBE3A	At1g55860 ⁺	1.5e-48	Putative ubiquitin-protein ligase 1 (UPL1)
Aniridia-PAX6	At4g36740 ⁺	2.7e-05	HOMEBOX PROTEIN 40 (ATHB40)
Ceroid-Lipofuscinosis-PPT	At4g17470 ⁺	1.3e-40	Palmitoyl protein thioesterase family
Choroideremia-CHM	At5g09550 ⁺	6.7e-38	GDP dissociation inhibitor (RAB)
Deafness, Hereditary-MYO15	At2g31900 ⁺	8.5e-146	Motor (AtXIF)
Deafness, X-Linked-TIMM8A	At5g50810 ⁺	1.2e-10	Transmembrane transporter (TIM8)
Diaphanous 1-DIAPH1	At1g31810 ⁺	2.0e-31	Actin binding
Dementia, Multi-Infarct-NOTCH3	At5g20350 ⁺	1.3e-08	Tip growth defective 1 (TIP1)
Duchenne MD+-DMD	At5g41790 ⁺	1.6e-23	COP1-INTERACTIVE PROTEIN 1 (CIP1)
Emery-Dreifuss MD+-LMNA	At5g16730	6.4e-7	Putative protein
Familial Encephalopathy-PI12	At2g25240 ⁺	6.4e-39	Putative serpin
Friedreich Ataxia-FXN	At4g03240	8.4e-21	FRATAXIN HOMOLOG (ATFH)
Limb Girdle MD+2A-CAPN3	At1g55350	1.4e-54	Cysteine-type endopeptidase (ATDEK1)
Limb Girdle MD+2B-YSF	At5g11100 ⁺	7.5e-08	C2 domain-containing protein
Lowe Oculocerebroren-OCRL	At1g34120 ⁺	3.9e-51	Inositol trisphosphate phosphatase (AtIP5PI)
Machado-Joseph-MJD1	At3g54130 ⁺	1.1e-39	Josephin family-like protein
Miller-Dieker Lissen-PAF	At3g49660 ⁺	2.9e-34	WD-40 repeat family protein
Myotonic Dystrophy-DM1	At2g20470 ⁺	4.8e-72	Kinase
Myotubular Myopathy 1-MTM1	At3g10550 ⁺	1.8e-65	Phosphatase
Oculopharyngeal MD+-PABPN1	At5g51120 ⁺	3.1e-30	PABP family protein (AtPABN1)
Oguchi Type 2-RHKIN	At3g08730 ⁺	1.9e-51	Putative ribosomal-protein S6 kinase (ATPK6)
Parkinson-SNCA (PARK1=PARK4)	At3g05620	2.9e-01	Pectinesterase family protein
Parkinson-Parkin (PARK2)	At1g05890 ⁺	2.1e-12	Putative RING zinc finger protein
Parkinson-SFXN5 (PARK3)	At5g12400	2.6e-01	Putative PHD finger transcription factor
Parkinson-UCHL1 (PARK5)	At4g17510	4.3e-40	Ubiquitin thioesterase (UCH3)
	At5g16310	1.6e-12	UCH1
	At1g65650	3.3e-10	UCH2
Parkinson-PINK1 (PARK6)	At1g73660 ⁺	1.3e-08	Protein kinase family
Parkinson-DJ-1 (PARK7)	At3g14990	6.9e-26	AtDJ-1a
	At1g53280	1.2e-28	AtDJ-1b
	At4g34020	6.7e-23	AtDJ-1c
Parkinson-LRRK2 (PARK8)	At4g39400 ⁺	4.0e-30	Protein kinase (AtBRI1)
Parkinson-ATP13A2 (PARK9)	At5g23630 ⁺	4.6e-51	ATPase E1-E2 type family protein
Parkinson-GIGYF2 (PARK11)	At5g42950	2.0e-07	GYF-domain containing protein
Parkinson-HTRA2 (PARK13)	At5g27660 ⁺	8.1e-55	Endopeptidase
Parkinson-PLA2G6 (PARK14)	At2g03430 ⁺	1.8e-18	Ankyrin repeat family protein
Parkinson-FBXO7 (PARK15)	At1g23780	4.5e-11	F-box family protein
Retinitis Pigmentosa-RPGR	At5g63860 ⁺	5.0e-39	Guanyl-nucleotide exchange factor (UVR8)
Retinitis Pigmentosa 2-RP2	At4g39920	7.3e-15	POR
SCA ⁺ 2-SCA2	At1g54170 ⁺	1.5e-09	CTC-Interacting Domain 3 (CID3)
SCA ⁺ 6-CACNA1A	At4g03560	1.1e-09	Two-pore channel 1 (AtTPC1)
Stargardt's-ABCA4	At2g41700	2.7e-170	ATPase
Tay-Sachs-HEXA	At1g65590 ⁺	1.6e-72	BETA-HEXOSAMINIDASE (AtHEX1)
Thomsen-CLCN1	At5g26240 ⁺	5.1e-34	Chloride channel protein (AtCLC-D)
Wilson-ATP7B	At5g44790 ⁺	7.4e-181	ATP dependent copper transporter (RAN1)

2009 – Identification of *AtPreP1* and *AtPreP2* genes coding for enzyme pre-sequence protease PreP



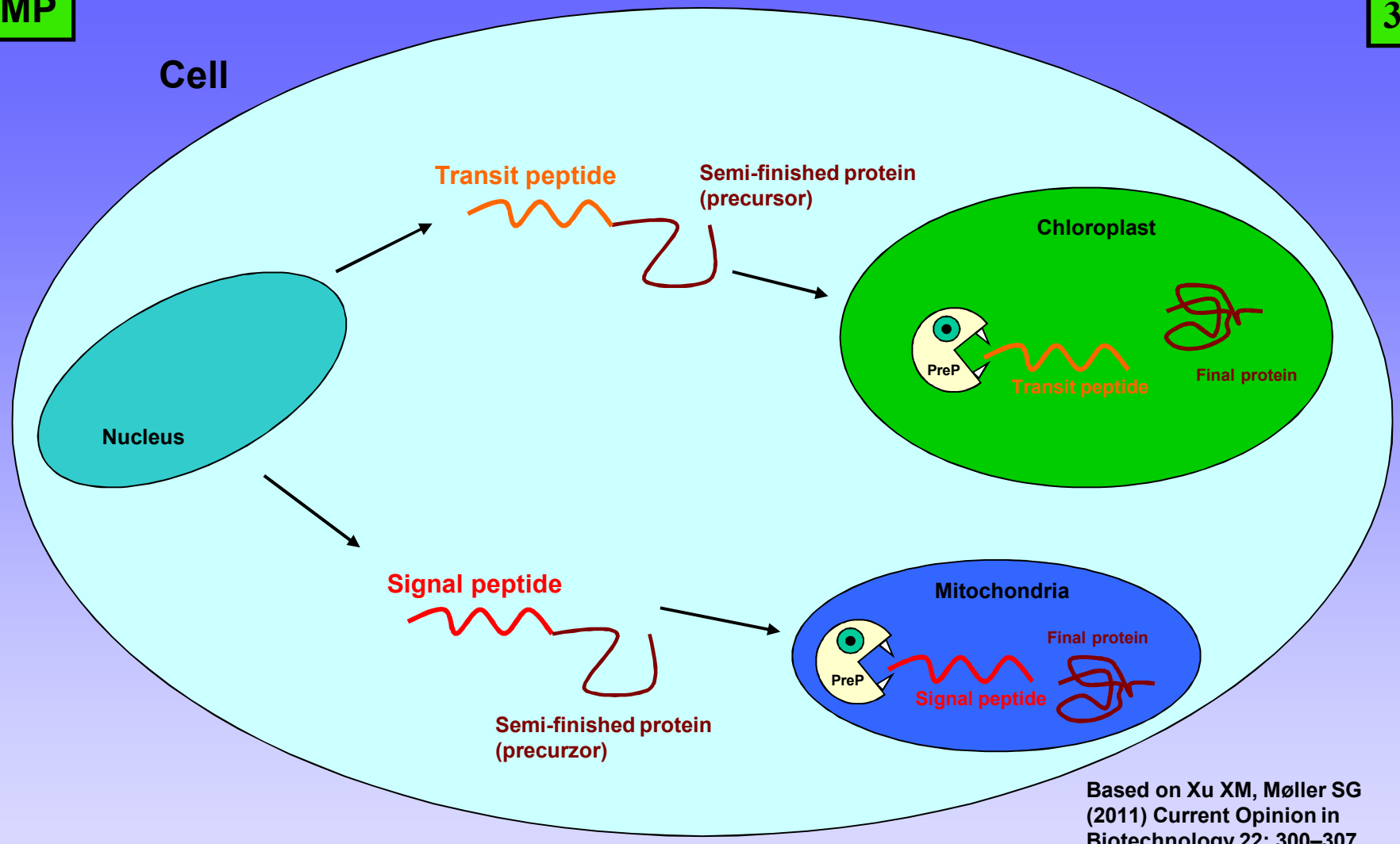
Cederholm SN et al. (2009) Plant Molecular Biology 71:497–508

Double mutant *atprep1 atprep2* shows a chlorosis and retarded growth.

PreP destroys target peptides:

➤ Transit peptides in chloroplasts

➤ Signal peptides (pre-sequence) in mitochondria



Based on Xu XM, Møller SG (2011) Current Opinion in Biotechnology 22: 300–307

Transit peptides and signal peptides are toxic for mitochondria and chloroplasts.

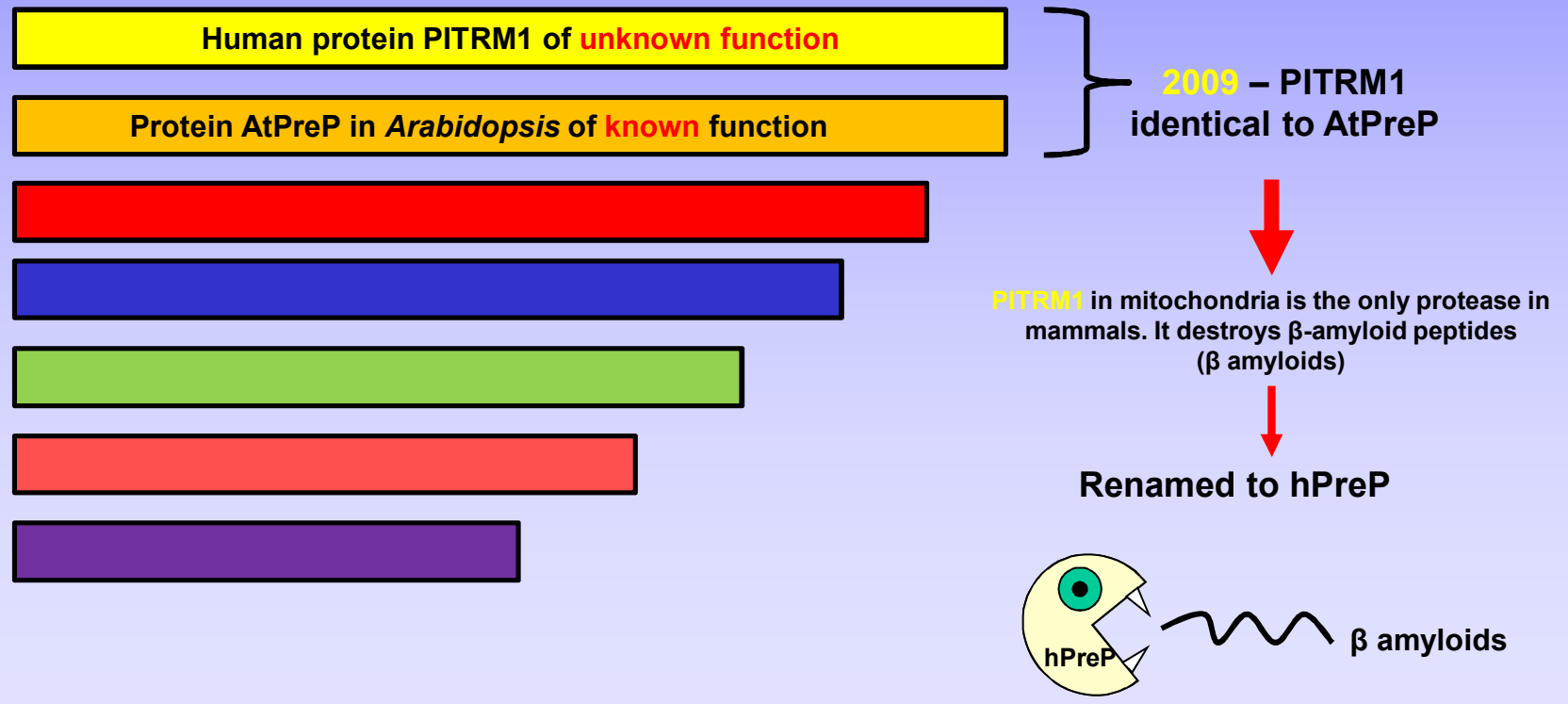


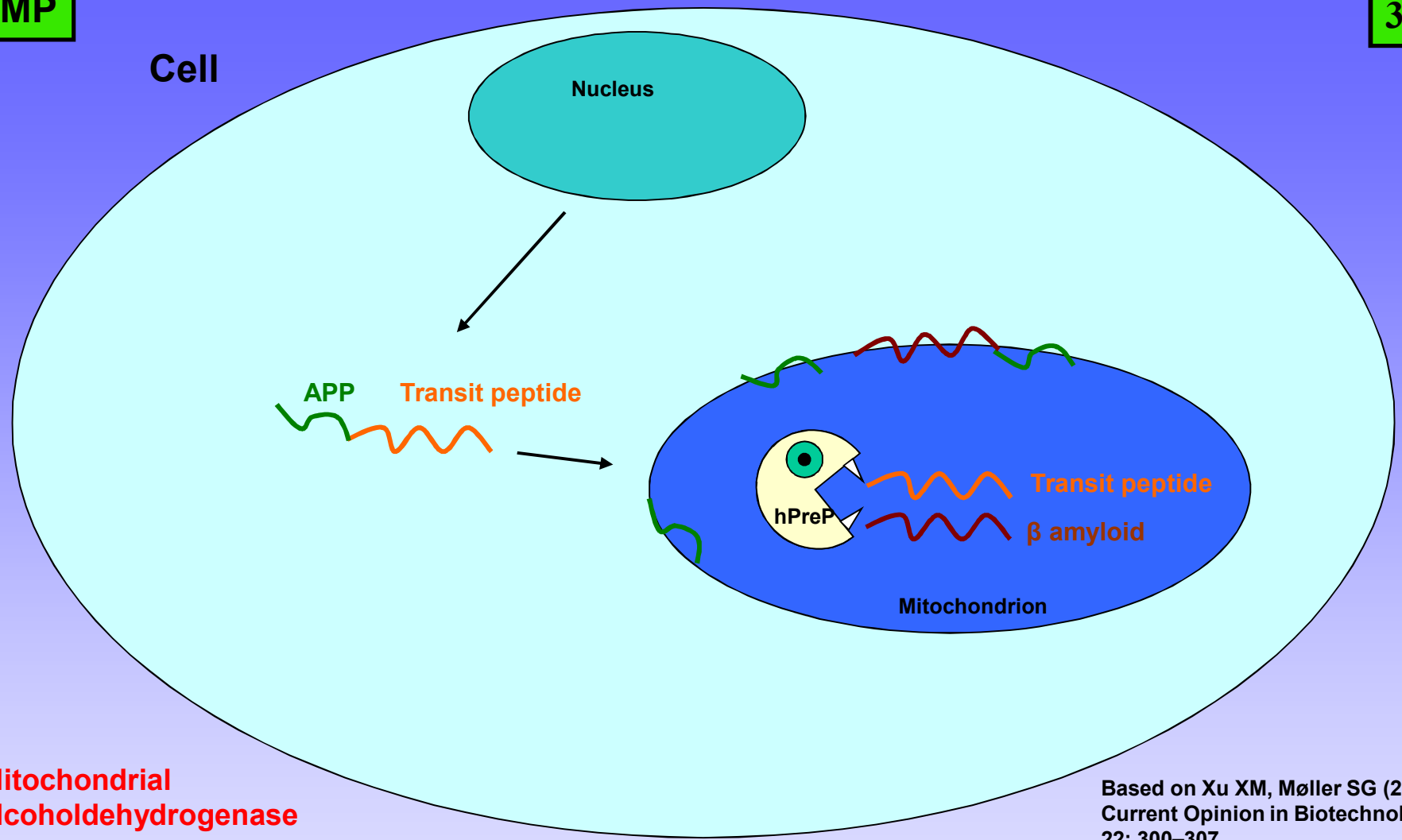
Peptides are digested by protein PreP



2000 – Identification of human protein **PITRM1** in mitochondria; function in cell unknown

Comparison of protein **PITRM1** with proteins AtPrep1 and AtPreP2 in protein databases. Based on the knowledge of the function of AtPrep1 and AtPreP2 function of PITRM1 was revealed.





**Mitochondrial
alcoholdehydrogenase**

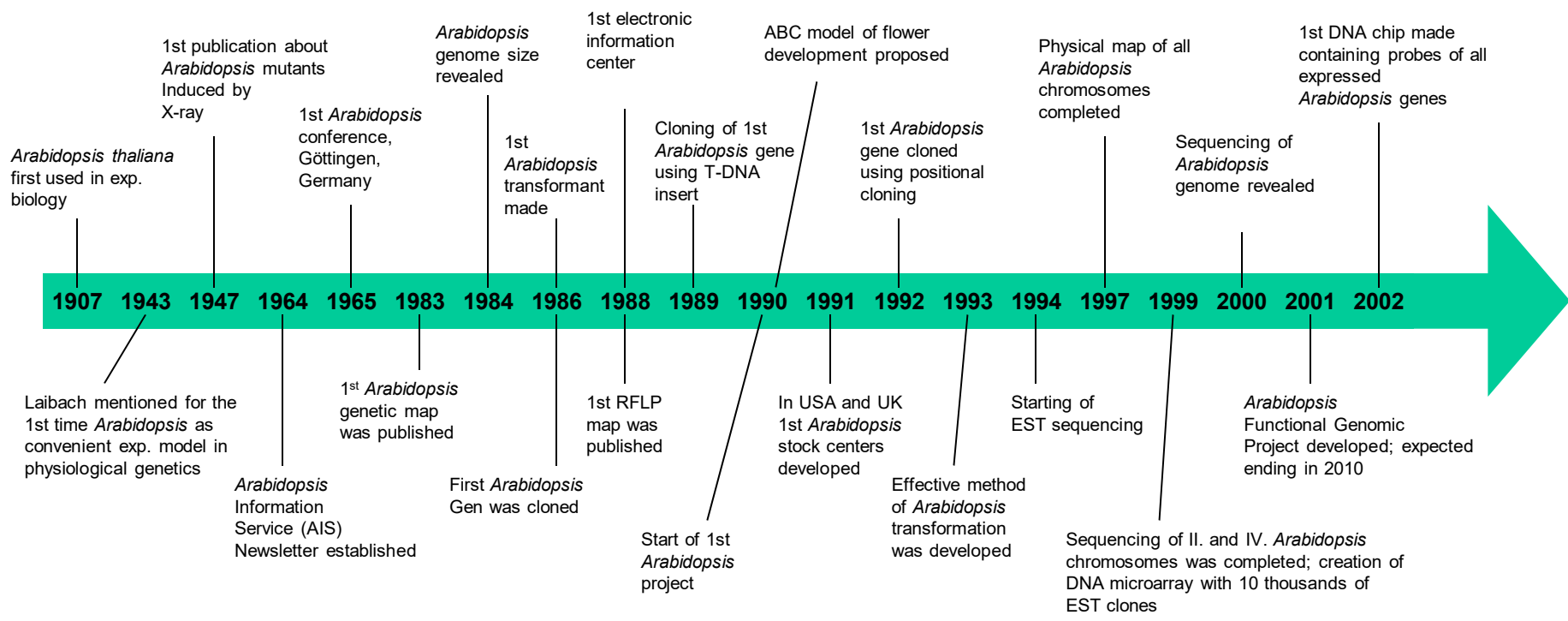
Based on Xu XM, Møller SG (2011)
Current Opinion in Biotechnology
22: 300–307

Transit peptides and β amyloids are toxic for mitochondria



Transit peptides and β amyloids are degraded by protein hPreP

Key events in *Arabidopsis thaliana* research.



Detailed chronology of *Arabidopsis* research

<http://www.arabidopsis.com/main/tbl/chronology.htm>



8) Databases

Arabidopsis databases



Eva Huala (USA) (TAIR)

TAIR = The *Arabidopsis* Information Resource: <http://www.arabidopsis.org>

Possibilities of these databases:

General search

Obtaining plant material (seeds, DNA,...)

Nottingham *Arabidopsis* Stock Center (**NASC**): <http://arabidopsis.info/>

Arabidopsis Biological Resource Center (**ABRC**): <http://abrc.osu.edu/>



Sean May (UK)
(NASC)

Tools

BLAST: <http://www.arabidopsis.org/Blast/>

SeqViewer: <http://tairvm09.tacc.utexas.edu/servlets/sv>

Links to other webs, further information, news, etc.



Randy Scholl (USA)
(ABRC)

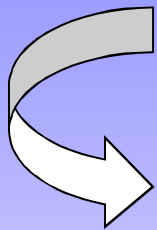
Overview of *Arabidopsis* sources: <http://www.arabidopsis.com/main/res/resource.html>

The *Arabidopsis* Book:

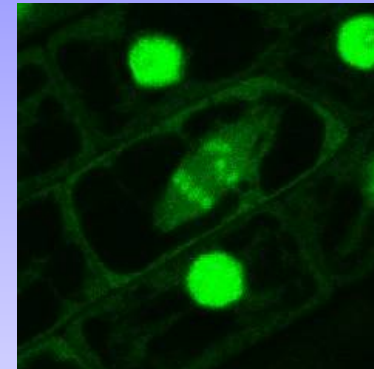


**American Society
of Plant Biologists**

Online, free !!



<http://www.aspb.org/publications/arabidopsis/>



This electronic book, **The Arabidopsis Book (TAB)**, ISSN: 1543-8120, is an attempt at a new mode of communication between researchers and a new model for scientific publishing. **TAB** in its initial stage is a compilation of over 100 invited chapters, each reviewing in detail an important and interesting aspect of the plant *Arabidopsis thaliana*, with reference to what is known in other plants and in other kingdoms. **TAB** is available only via the Internet and will be available free of charge. The American Society of Plant Biologists is providing funds for the mounting and maintenance of the book on the Internet as a public service. [View and search full-text at BioOne](#)

General databases

GABI = Genome Analysis of the Plant Biological System: <http://www.gabi.de>

PlaNet = A Network of European Plant Databases: <http://www.eu-plant-genome.net/>

Information about genomes, information about sequences, literature sources, etc.

NCBI = National Center for Biotechnology Information: <http://www.ncbi.nlm.nih.gov>

TCAG = The Center for the Advancement of Genomics (previously TIGR):

<http://www.jcvi.org/cms/home/>

Kazusa DNA Research Institute: <http://www.kazusa.or.jp/e/>



Literature cited

Mulligan B, Anderson M (1995) *Arabidopsis thaliana*: a versatile plant for teaching and research projects in genetics and plant biology. *J Biol Education* 29: 259 – 269.

Wilson ZA (2000) *Arabidopsis*. A practical approach. Oxford University Press.

Somerville C, Koornneef M (2002) A fortunate choice: the history of *Arabidopsis* as a model plant. *Nature Reviews* 3: 883 – 889.

The multinational coordinated *Arabidopsis* genomics project, MASC (2002).

Alberts B et al. (2004) *Essential cell biology*. 2nd ed., Garland Science Publishing.

Jones AM et al. (2008) The impact of *Arabidopsis* on human health: diversifying our portfolio. *Cell* 133: 939-943

Cederholm SN et al. (2009) Deletion of an organellar peptidase PreP affects early development in *Arabidopsis thaliana*. *Plant Mol Biol* (2009) 71:497–508

Alikhani N et al. (2009) Mitochondria and Alzheimer's disease: amyloid-beta peptide uptake and degradation by the presequence protease, hPreP. *J Bioenerg Biomembr* 41: 447-451

Koornneef M, Meinke D (2010) The development of *Arabidopsis* as a model plant. Plant Journal 61: 909-921

Buell CR, Last RL (2010) Twenty-first century plant biology: Impacts of the *Arabidopsis* genome on plant biology and agriculture. Plant Physiology 154: 497-500

Xu XM, Møller SG (2011) The value of *Arabidopsis* research in understanding human disease states. Current Opinion in Biotechnology 2011, 22:300–307

Gross M (2012) Understanding amyloid and Alzheimer's disease. Current Biology 22: R381-R384

Harter K, Weber APM (2013) Arabidopsis 2010 and beyond – big science with a small weed. Frontiers in Plant Science 4: 1

Rhee SY, Mutwil M (2013) Towards revealing the functions of all genes in plants. Trends in Plant Science 19: 212-221