ERC- A case report

A mission impossible? - No!

Easy to succeed? - No!

Many hurdles to jump over ? - Yes!

Possible without the help of experienced people? - No!

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German Research Center for Environmental Health

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ERC – My first contact: April 2009 – at the University of Zürich

- „Appr. 5-7% of all applicants are successful.“

- „If you do not have high profile papers published as first author it will become very difficult (Nature, Science, Cell).“

- „In most cases a last authorship is of advantage.“

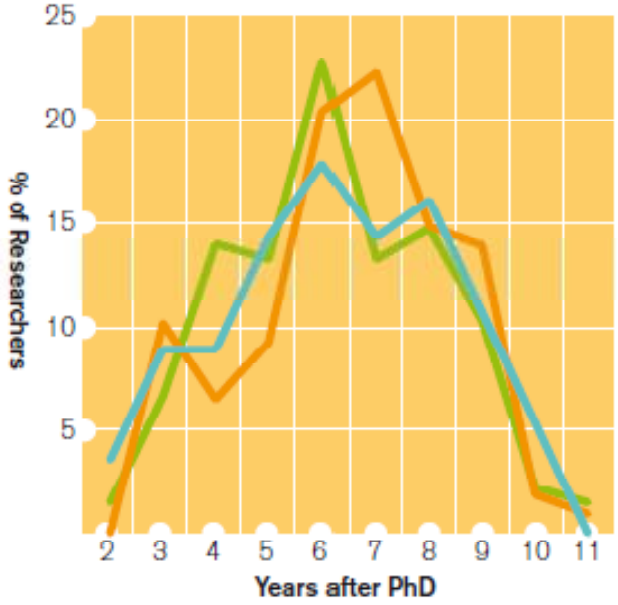
- „This year we had more applicants than last year.“

ERC – My second contact: summer 2009 - KOWI - Helmholtz München

Christian Gast (KOWI) and Dr. Mitzka-Schnabel (Helmholtz-Zentrum München)

Grantees' profile:
years after PhD and domain

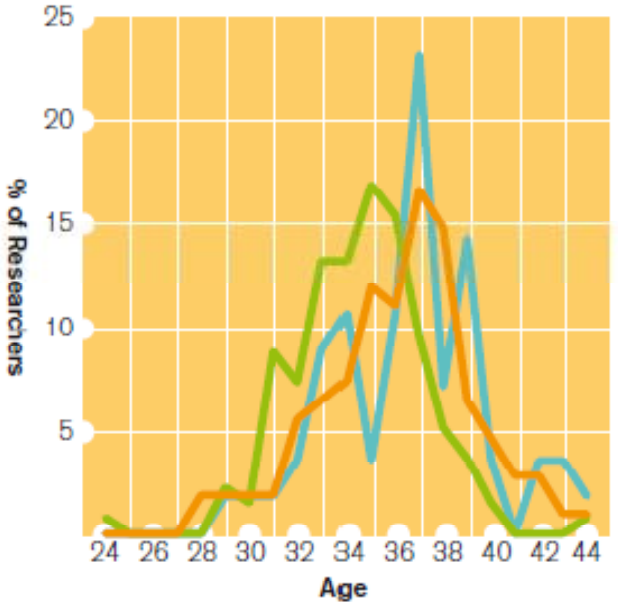
The greatest number of principal investigators completed their PhD studies between five to eight years before applying for a Starting Grant, irrespective of the domain.



Source: Top 300 proposals

Grantees' profile: age and domain

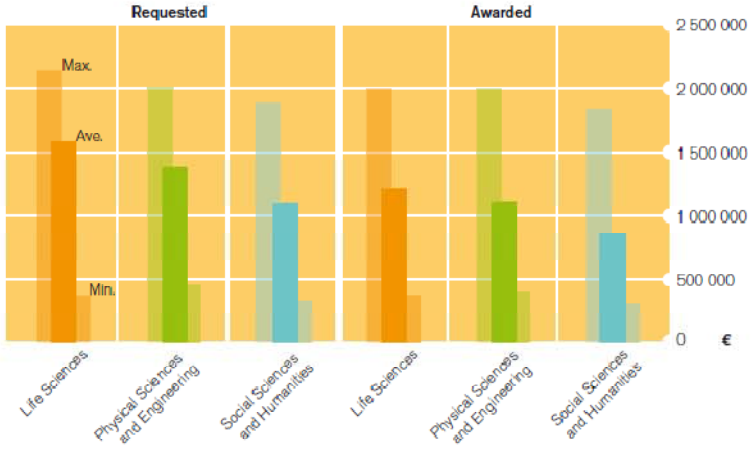
The average age of the principal investigators varies across the domains: Physical Sciences and Engineering (34.5 years); Life Sciences (36 years); Social Sciences and Humanities (36.5 years).



Source: Top 300 proposals

Requested and awarded project budgets: maximum, average and minimum amounts

Project budgets range from € 300 000 up to a max of € 2 million; this is largely independent of the domain.



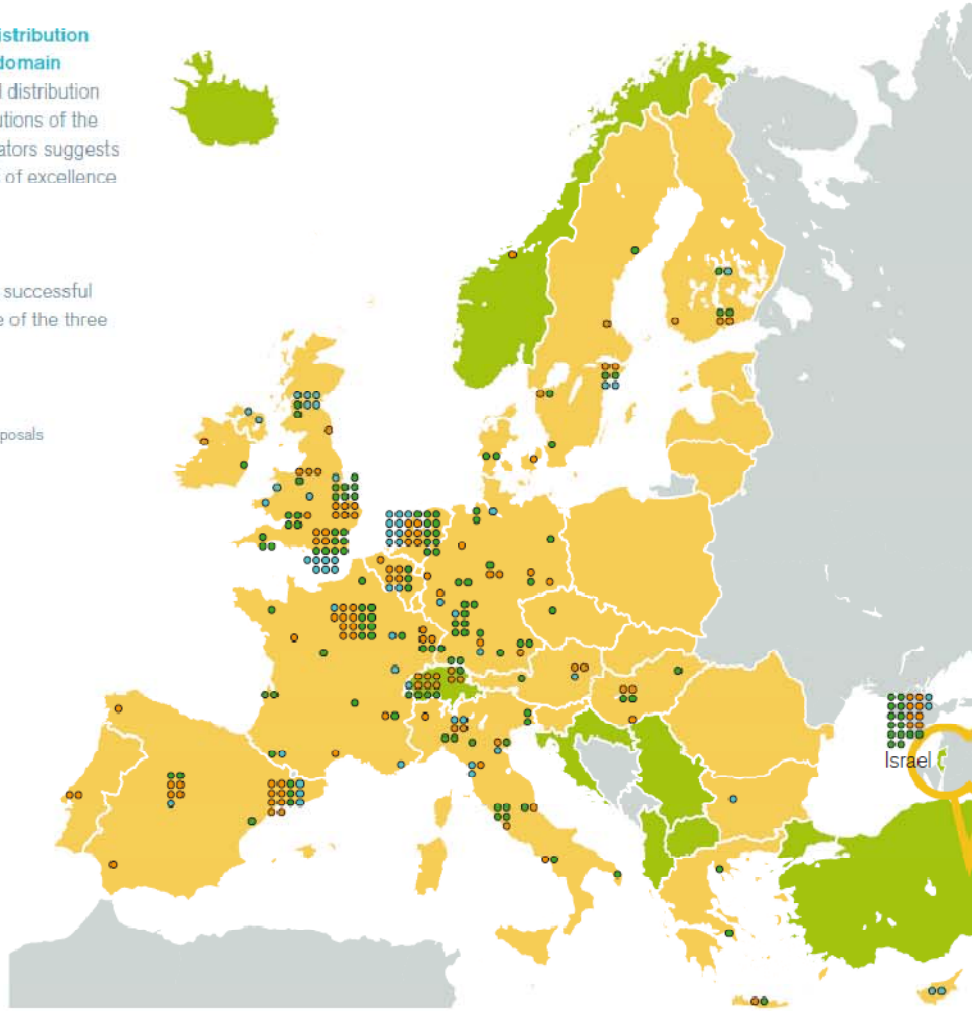
Source: Top 300 proposals

Geographical distribution of grantees by domain

The geographical distribution of the host institutions of the principal investigators suggests potential clusters of excellence in Europe.

A dot indicates a successful application in one of the three domains.

Source: Top 300 proposals



ERC – Decision – I will apply: August/September 2009

Dr. Ertel and Dr. Mitzka-Schnabel

- Generation of an account/ first offical contact with ERC (help through home-institution)

- Which panel should I join? (An important decision…)

- Two Parts have to be finished at once…

- Part B1 and B2 (Help is crucial!)

- Part B1 (Personal excellence)

- Part B2 (Excellence of the research program) / budget/
  ethical issues/ specific contracts with the home institution / responsibilities of the home institution…etc.

The panel (look who is the chair – who is in…)

LIFE SCIENCES

LS1 Molecular and Structural Biology and Biochemistry: Prof. Reinhard Jahn
LS2 Genetics, genomics, bioinformatics and systems biology: Prof. Marja Makarow
LS3 Cellular and Developmental Biology: Prof. Christer Betsholtz
LS4 Physiology, Pathophysiology and Endocrinology: Prof. Ole H. Petersen
LS5 Neurosciences and neural disorders: Prof. Andrea Kleinschmidt
LS6 Immunity and infection: Prof. Maria Grazia Roncarolo
LS7 Diagnostic tools, therapies and public health: Prof. Hans Bräuner-Osborne
LS8 Evolutionary, population and environmental biology: Prof. Lars Chittka
LS9 Applied life sciences and biotechnology: Prof. Francisco Tomás-Barberán

SOCIAL SCIENCES AND HUMANITIES

SH1 Individuals, institutions and markets: Prof. Jordi Galí
SH2 Institutions, values, beliefs and behaviour: Prof. Ronald Rogowski
SH3 Environment and society: Prof. Mark Rounsevell
SH4 The human mind and its complexity: Prof. Luciano Fadiga
SH5 Cultures and cultural production: Prof. Simon Goldhill
SH6 The study of the human past: Prof. Jane Burbank

DOMAIN PHYSICAL SCIENCE AND ENGINEERING

PE1 Mathematical foundations: Prof. Janusz Grabowski
PE2 Fundamental constituents of matter: Prof. Sune Svanberg
PE3 Condensed matter in physics: Prof. Yvan Bruynseraede
PE4 Physical and Analytical Chemical sciences: Prof. Philippe Sautet
PE5 Material and synthesis: Prof. Jeffrey Alan Hubbell
PE6 Computer science and informatics: Prof. Stefan Jähnichen
PE7 Systems and communication engineering: Prof. Palle Jeppesen
PE8 Products and process engineering: Prof. Ulrich Stimming
PE9 Universe sciences: Prof. Georges Meylan
PE10 Earth system science: Prof. Daniel Conley

How to write Part B1?

- self-aggrandisement?

- exaggerated?

- underestimation?

- Need to read a successful grant from someone else!

European Research Council

ERC Starting Grant
Research proposal (Part B1)

Uncovering the mechanisms of inflammation induced liver tissue destruction and carcinogenesis

LiverCancerMechanism

- **Principal investigator:** PD. Dr. Heikenwälder Mathias, Ph.D.
- **Host institution:** Helmholtz Zentrum München, Research Center for Environmental Health GmbH, Germany.

- **Proposal duration in months:** 60

Proposal summary

- Be concise / be to the point
- Be complete
- Be different
- Strategical thinking – What is really needed to be put in what not?
- What shows my excellence?
- How can I sell myselfy/ my excellence best?
- Translational aspects?

1(a) Scientific Leadership Potential

The beginning of my scientific career was stimulated during my studies by the attendance of a course on cellular biology organized by Prof. Dr. Martin Zenke at the **Institute of Molecular Pathology (IMP)**, Vienna, Austria. I learned to differentiate dendritic cells out of peripheral blood derived progenitor cells *in vitro* and how hormones regulate transdifferentation of omni-potent progenitor cells. This raised my interest how vertebrates produce hormones in the context of environmental and developmental stimuli affecting a plethora of vital functions. I therefore - after successful application for an **Erasmus studentship** in 1999 - performed my **diploma thesis** on thyorid hormone regulated genes in the laboratory of Prof. Dr. Martin Zenke at the **Max-Delbrück Center (MDC)**, Berlin, Germany. There, I worked on the identification and characterization of a thyroid hormone regulated gene family, consisting of the gene tub (for tubby) and tubby like proteins (tulps) in chicken and rat as model organisms. In the frame of my Diploma thesis I cloned and characterized tulp1 in chicken and rats **(1)** which was found to be expressed in various brain regions as well as in the retina **(2)**. Further, I demonstrated that hypothyroidism in rats altered tub mRNA and protein expression in discrete brain areas. This provided a novel molecular link between thyroid status and the tubby-associated syndromes, caused by mutations in various members of the tub gene family. The methodological knowledge in working with animals was of great value for my career and the stay in Prof. Dr. Martin Zenke's laboratory was of exceptional educational and personal benefit for me.

Figures are supportive

1(c) Early Achievement-Track-Record

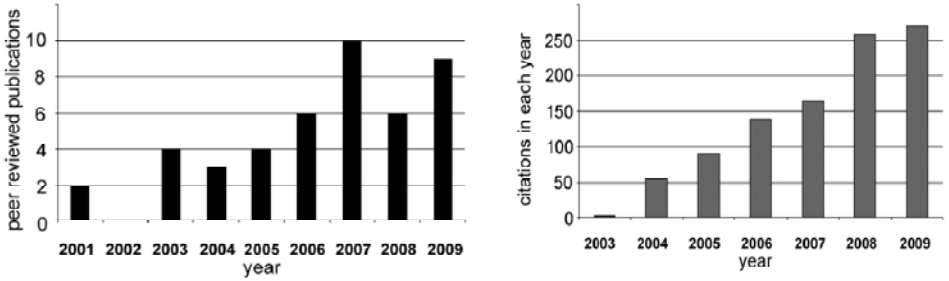


Figure 1: *The graphs describe peer reviewed publications and citations in each year from the start of my scientific career in 1999 until November 2009.* ***Left graph:*** *Peer reviewed publications from 2001 to 2009. Altogether 43 peer reviewed papers were published.* ***Right graph:*** *Citations from 2003 to 2009. Up to date my scientific publications were cited 981 in total. The average citation per publication: 22.8.*

The full list of my current publications is available under:
http://www.ncbi.nlm.nih.gov/sites/entrez?cmd=PureSearch&db=pubmed&term=heikenwalder%20M%5BAuthor%20Name%5D
Further details about my research are available under:
http://www.neuropathologie.usz.ch/PatientenUndBesucher/HeikenwalderLab/Seiten/default.aspx

List of selected original publications

1. Achim Weber*, Regina Boger*, Binje Vick, Toni Urbanik, Johannes Haybaeck, Stefan Zoller, Andreas Teufel, Peter Krammer, Joseph Opferman, Peter Galle, Marcus Schuchmann, **Mathias Heikenwalder,** Henning Schulze-Bergkamen. 'Hepatocyte-specific deletion of Mcl-1 triggers proliferation and hepatocarcinogenesis in mice'. **Hepatology,** in press, 2009. (IF°: 11.35)

2. Johannes Haybaeck*, Nicolas Zeller*, Monika Julia Wolf, Achim Weber, Ulrich Wagner, Michael Odo Kurrer, Juliane Bremer, Giandomenica Iezzi, Rolf Graf, Pierre-Alain Clavien, Robert Thimme, Hubert Blum, Sergei A. Nedospasov, Kurt Zatloukal, Muhammad Ramzan, Sandra Ciesek, Thomas Pietschmann, Patrice N. Marche, Michael Karin, Manfred Kopf, Jeffrey L. Browning, Adriano Aguzzi and **Mathias Heikenwalder**. 'A lymphotoxin-driven pathway to chronic hepatitis induced liver cancer'. **Cancer Cell** 16, 1-14, 2009. (IF: 24.96)

3. **Mathias Heikenwalder** et al., 'Lymphotoxin-dependent prion replication in inflammatory stromal cells of granulomas'. **Immunity** 29, 998-1008, 2008. (IF: 20.57)

4. Stefan Baenziger*, **Mathias Heikenwalder***, et al., 'Triggering TLR7 in mice induces immune activation and lymphoid system disruption, resembling HIV-mediated pathology'. **Blood** 113, 377-88, 2008. (IF:10.43).

5. **Mathias Heikenwalder***, Marco Prinz*, et al., 'Overexpression of Lymphotoxin in T Cells Induces Fulminant Thymic Involution'. **The American Journal of Pathology** 172, 1555-70, 2008. (IF: 5.6)

Figures are supportive

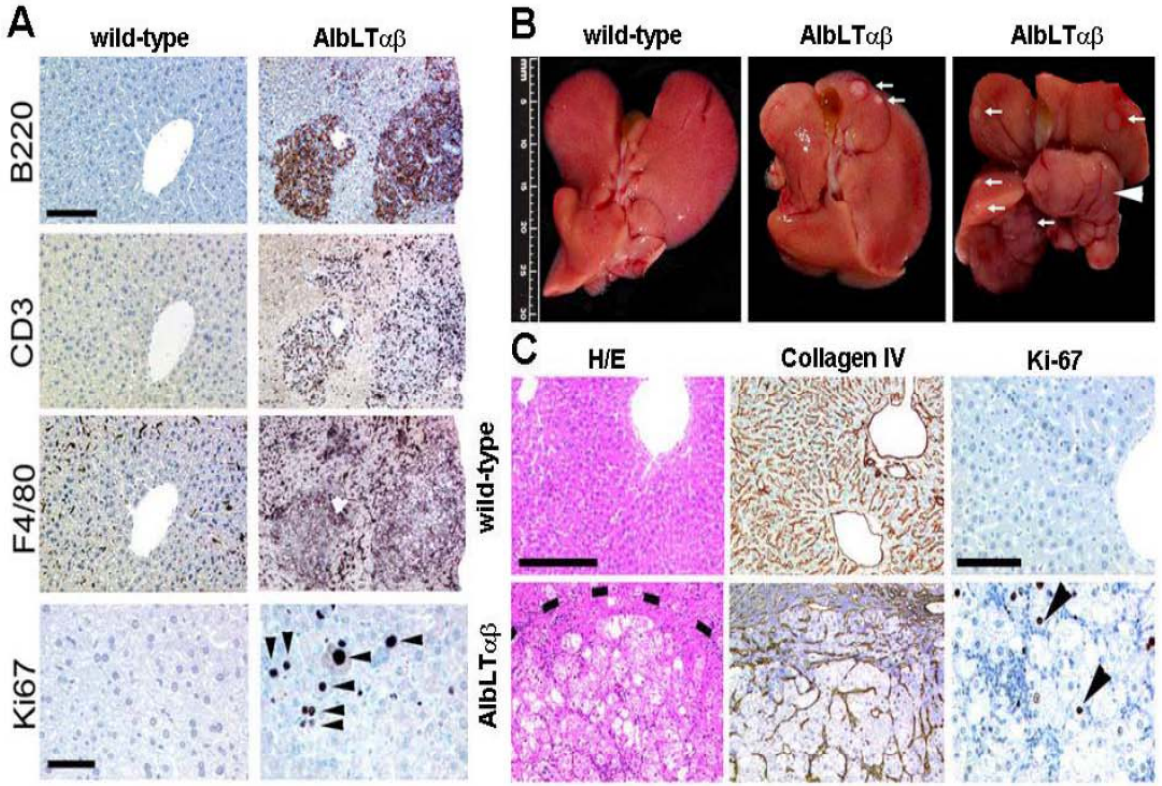
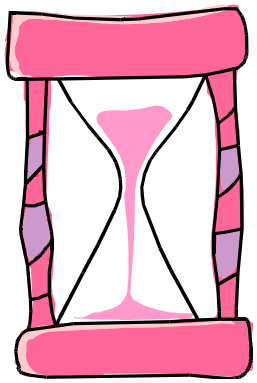
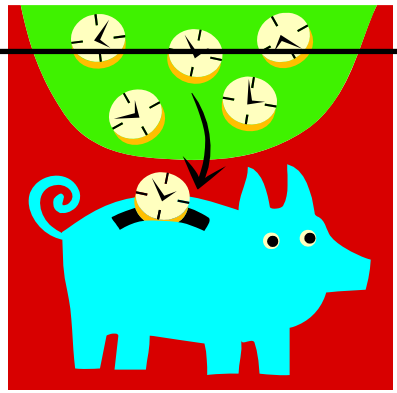


Figure 3: Development of chronic inflammation and hepatocellular carcinoma in mice with liver specific expression of LTα and LTβ. ***(A)*** *Immunohistochemical analysis of 9 month-old C57BL/6 and AlbLTαβ livers. $B220^+$ stained B-cells, $CD3^+$ T-cells, $F4/80^+$ macrophages, Kupffer cells and $A6^+$ oval cells (scale bar: 150μm). $Ki67^+$ proliferating hepatocytes (arrow heads) and inflammatory cells are indicated (scale bar: 50μm).* ***(B)*** *Macroscopy of livers at the age of 12 (middle panel) and 18 months (right panel). White arrows indicate tumor nodules. White arrowhead indicates a liver lobe completely affected by HCC.* ***(C)*** *Histological analysis of livers derived from C57BL/6 and AlbLTαβ mice. Dashed line depicts the HCC border. Collagen IV staining highlights the broadening of the liver cell cords and loss of collagen IV networks indicative of HCC in AlbLTαβ mice (scale bar: 200μm). $Ki67^+$ proliferating hepatocytes (arrowheads) are only found in AlbLTαβ HCC (scale bar: 100μm).*

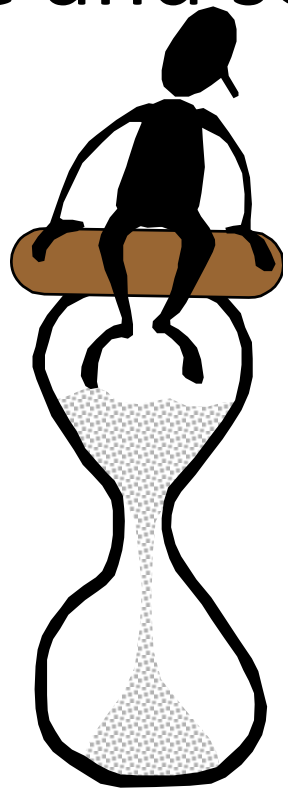
Time managment

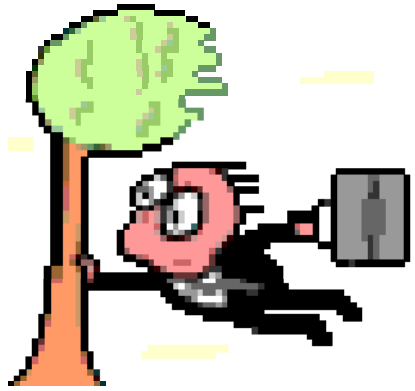


Final corrections



Deadline and sending off





Send off, work and wait…

- Official invitation letter to Brussels by ERC
- Presentation (How: Slides /Poster? How long? Print-outs for the panel yes or no etc.)

  Is indicated in the invitation letter.
- Part B2 is important for the interview and evaluation of your proposed research project
- Part B2 sent to external referees
- In my case 10 minutes presentation - 20 discussion.

Brussels…

- How to dress?
- When to arrive? (same day / at the day before)
- Need help to prepare your talk perfectly:

Important points

- Excellence of presentation
- Scientific Context

- Should I show budgest issues?
- Start with a CV?
- Who finally is in the panel in Brussels?
- How do the rooms look like?

Prepration of the presentation

KOWI course in Bonn - which aims at perfectionizing your presentation!!

Professional training: Dr. Löhke

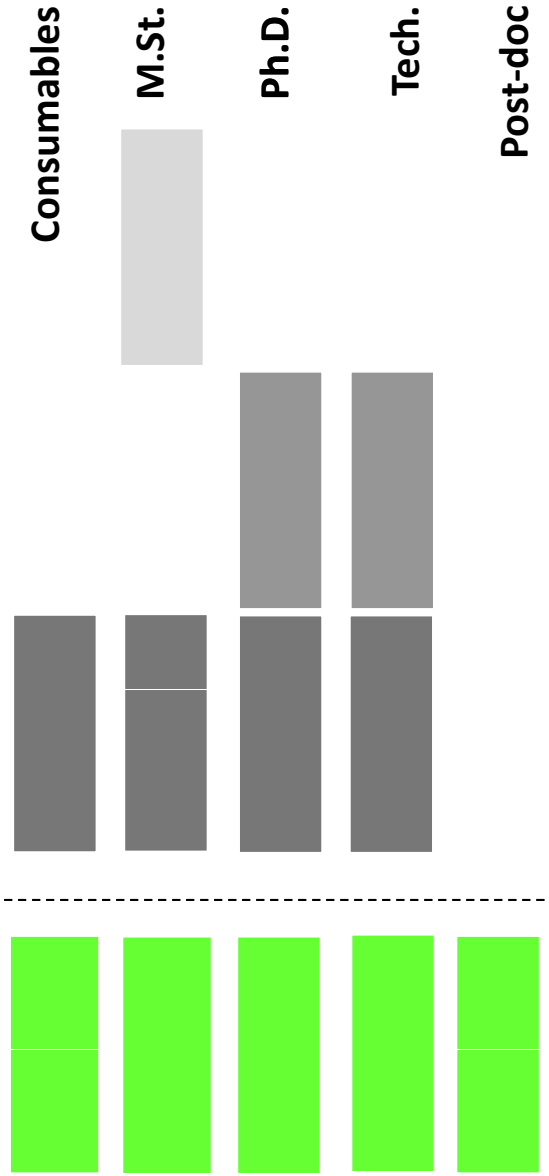
- how to present yourself
- how to present your data
- nominees are in the audience and give positive/neagtive critique also scientific input
- critical discussion of your presentation in terms of : „Did you transport your message?“
- „speed, clarity, red line“ will be discussed.

- **Big advantage**: You start preparing the presentation way ahead of time.

Education and Professional Experience

Level	*Publications/ funding*		*Research field*
Diploma	Gene, 2001 EMBO, 2001	**Erasmus**	**Cellular Biology**
Ph.D.	Nature, 2003 Nat. Med., 2004 Science, 2005 Science, 2005	**Catello**	**Neuroimmunology**
Post.doc	AJP, 2007 Journal of Neurosc., 2007 Journal of Neuroim., 2007 Nat. Neurosicence, 2007 Blood, 2008 Immunity, 2008	**Bonizzi-Theler** **Med. Fac. Zurich**	**Neuroimmunology** **Inflammation** **Immunology**
Independent Researcher	Cancer CELL, 2009 Cancer CELL, 2010 Hepatology, 2010	**Clöetta** **Oncosuisse** **Helmholtz**	**Inflammation** **Cancer**
Independent Researcher ERC			**Inflammation** **Tissue destruction** **Cancer**

Supervision/workforce



Discussion after the talk in Brussels

- No questions that were budget related!
- In detail questions from various panel members!
- Positive input but also questioning the likelyhood of success.
- Friendly atmosphere – small lecture room.

- Awaiting the panel and reviewer reports.
- If positive negotiations with ERC start .