Good Scientific Practice
Protecting Scientific Integrity

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DESY
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Terminology

- Good Scientific Practice (GSP)
- Responsible Conduct of Research (RCR)
- Research Ethics
- Research Integrity
- Scientific Integrity

- Scientific/Research misconduct
- Misconduct in science

Rules of Good Scientific Practice – Why?
The “Herrmann-Brach-Case” (1997)

Consequences

An international DFG commission “with the mandate,

- to explore causes of dishonesty in the science system,
- to discuss preventive measures,
- to examine the existing mechanism of professional self-regulation in science and to make recommendations on how to safeguard them.”

DFG Recommendations 2013, p. 62

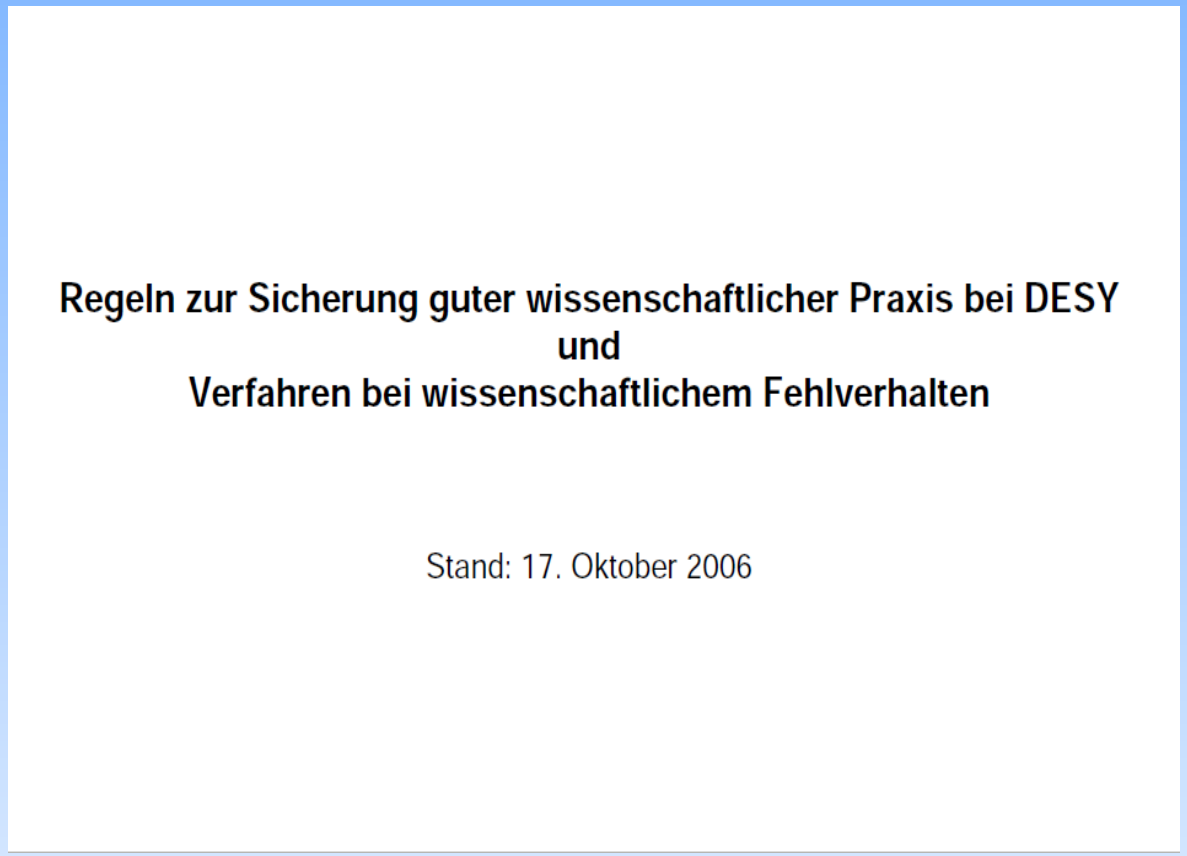
Proposals for Safeguarding Good Scientific Practice

Recommendations of the Commission on Professional Self Regulation in Science

DFG 1998/2013

Consequences

- Local guidelines, regulations, statutes and by-laws for safeguarding Good Scientific Practice
- Legal norms on GSP at every university, Max-Planck, Helmholtz and Leibniz institute
- Institutions to contact in case of suspected misconduct
- Commissions with rules for investigation



Guidelines for Safeguarding Good Scientific Practice at DESY

What is Good Scientific Practice?

- Observing professional standards
- Documenting results
- Consistently questioning one‘s own findings
- Practising strict honesty with regard to the contributions of partners, competitors, and predecessors
- Mentorship for young scientists and scholars
- Securing and storing of primary data

DFG Recommendations 2013, p. 69

Datamanagement: Please discuss…

…with your supervisor/mentor/PI/director:

- Who owns the data that you generate?
- What does that mean for you and the data?
- Who can use the data that you generate?
- Who stores the data (after you will have left)?
- For how long will the data be stored?
- Can you take a copy of your data?

Because…

“The published reports on scientific misconduct are full of accounts of vanished original data and of the circumstances under which they had reputedly been lost. This, if nothing else, shows the importance of the following statement:

The disappearance of primary data from a laboratory is an infraction of basic principles of careful scientific practice and justifies a prima facie assumption of dishonesty or gross negligence.”

DFG Recommendations 2013, p. 75f

Because…

…if there is doubt about your data and you cannot prove that your published data are real or that you made a mistake, you might get a retraction – or worse.

The EMBO Journal (2007) 26, 1410–1422 | © 2007 European Molecular Biology Organization | All Rights Reserved 0261-4189/07
www.embojournal.org

THE EMBO JOURNAL

Ubiquitination of the GTPase Rap1B by the ubiquitin ligase Smurf2 is required for the establishment of neuronal polarity

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The development of a polarised morphology with multiple dendrites and a single axon is an essential step in the differentiation of neurons. The establishment of neuronal polarity is directed by the sequential activity of the GTPases Rap1B and Cdc42. Rap1B is initially present in all neurites of unpolarised neurons, but becomes restricted to the tip of a single process during the establishment of neuronal polarity where it specifies axonal identity. Here, we show that the ubiquitin ligases Smad ubiquitination regulatory factor-1 (Smurf1) and Smurf2 are essential for neurite growth and neuronal polarity, respectively, and regulate the GTPases Rho and Rap1B in hippocampal neurons. Smurf2 is required for the restriction of Rap1B to a single neurite. Smurf2 ubiquitinates inactive Rap1B and initiates its degradation through the ubiquitin/proteasome pathway (UPS). Degradation of Rap1B restricts it to a single neurite and thereby ensures that neurons extend a single axon.

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Subject Categories: cell & tissue architecture; neuroscience
Keywords: GTPase; neuronal polarity; ubiquitin

Introduction

Primary cultures of dissociated neurons are a well-established system to study the development of neuronal polarity and have facilitated the identification of signalling pathways essential for the first step in neuronal polarisation, the specification of axonal identity (Bradke and Dotti, 2000; Da Silva and Dotti, 2002; Wiggin *et al*, 2005). The differentiation of hippocampal neurons can be subdivided into five stages (Dotti *et al*, 1988). Unpolarised neurons initially form several equivalent neurites, which all have the potential to become an axon (stage 2). Neuronal polarity becomes apparent when a single neurite is selected from these processes to become the axon (stage 3).

The establishment of neuronal polarity is initiated by phosphatidylinositol-3-kinase (PI3K). Production of phosphatidyl-inositol-3,4,5-trisphosphate leads to the activation of Akt/PKB (Akt) and inactivation of glycogen synthase kinase 3β (GSK3β; Shi *et al*, 2003; Jiang *et al*, 2005; Yoshimura *et al*, 2005; Yan *et al*, 2006). This repression allows GSK3β targets like collapsin response mediator protein-2 (CRMP2) to promote axon extension (Inagaki *et al*, 2001; Zhou *et al*, 2004; Yoshimura *et al*, 2005). We have shown that the sequential activity of the GTPases Rap1B and Cdc42 is necessary and sufficient for the establishment of polarity in hippocampal neurons downstream of PI3K (Schwamborn and Püschel, 2004). Rap1B is initially present at the tips of all neurites of unpolarised early stage 2 neurons, but becomes restricted to a single neurite at late stage 2 (Schwamborn and Püschel, 2004). Rap1B is restricted to a single neurite of morphologically unpolarised neurons before the axon becomes distinguishable and other factors important for axon specification like the Par complex, phosphorylated atypical protein kinase C (aPKC), phosphorylated Akt, phosphorylated GSK3β, APC, or CRMP2 are restricted to the axon of stage 3 neurons (Inagaki *et al*, 2001; Shi *et al*, 2003; Schwamborn and Püschel, 2004; Shi *et al*, 2004; Jiang *et al*, 2005; Yoshimura *et al*, 2005; Yan *et al*, 2006).

The redistribution of Rap1B is an essential step in the establishment of neuronal polarity. However, it is unclear how the restriction of Rap1B to a single neurite arises from an initially symmetric localisation at the tip of all neurites. One possible mechanism is the selective degradation of Rap1B. The UPS is the major route that targets proteins for degradation in eukaryotic cells (Glickman and Ciechanover, 2002). UPS-mediated destruction is essential not only for removing misfolded proteins but also for the regulation of many signalling pathways. Ubiquitination is catalysed by a cascade of three enzymes, the ubiquitin-activating E1, the ubiquitin-conjugating E2, and the ubiquitin-protein E3 ligase. The E3 enzyme is responsible for determining which proteins are selected for modification. In neurons, the UPS is present in axonal growth cones and has been implicated in the regulation of axon guidance, synapse formation, and neuronal plasticity, as well as neurodegenerative processes and regeneration (Campbell and Holt, 2001, 2003; DiAntonio and Hicke, 2004; Konishi *et al*, 2004; van Roessel *et al*, 2004; Nakata *et al*, 2005). Here, we show that the UPS is required for the establishment of neuronal polarity. The HECT domain E3 ubiquitin ligases Smurf1 and Smurf2 coordinately regulate neurite extension and neuronal polarity through Rho and Rap1B, respectively. Smurf2 ubiquitinates inactive Rap1B and initiates its degradation through the proteasome. The degradation of Rap1B is essential to restrict it to a single neurite and to ensure that neurons extend only one axon.

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Authorship and Publication

“Authors of scientific publications are always jointly responsible for their content. Only someone who has made a significant contribution to a scientific publication is deemed to be its author. A so-called ‘honorary authorship‘ is inadmissible.“

DFG Recommendations 2013, p. 82

The Core of Scientific Misconduct

"Research misconduct is defined as **fabrication**, **falsification**, or **plagiarism** in proposing, performing, or reviewing research, or in reporting research results. (…)

Research misconduct does not include honest error or honest differences of opinion."

OECD Global Science Forum/US Government

Degrees of Scientific Misconduct

Sloppy work	Questionable practice	Severe misconduct

Carelessness	Bad statistics	FFP
Mislabelling	Salami slicing	Sabotage
Bad lab book	Intransparency	Destroying data
	Using expired chemicals	Data theft
	Hiding “negative” results	Ethics violation
		Fake authors
		Bad lab book

Ethical Principles and Values in Science

Honesty
Fairness
Objectivity
Responsibility
Independence
Carefulness
Communication
Confidentiality
Novelty

Credibility
Trust/trustworthiness
Openness
Self-Criticism
Accuracy
Reproducibility
Transparency
Accessibility
Collegiality

But…

How can we exercise honesty, fairness, objectivity, trust, etc., when we are in a conflict or dilemma?

Conclusions

1. **Read** – Read your institution’s documents on Good Scientific Practice.
2. **Communicate** – Talk to your colleagues about the Responsible Conduct of Research.
3. **Escalate** – In case of conflict: get professional help from the local ombudsperson or from the German Research Ombudsman (Berlin).

Further Reading on Good Scientific Practice

Safeguarding Good Scientific Practice
Recommendations of the Commission on Professional Self Regulation in Science
Deutsche Forschungsgemeinschaft DFG
http://www.dfg.de/download/pdf/dfg_im_profil/reden_stellungnahmen/download/empfehlung_wiss_praxis_1310.pdf

The European Code of Conduct for Research Intregrity – Revised Edition
ALLEA – All European Academies
http://www.allea.org/wp-content/uploads/2017/05/ALLEA-European-Code-of-Conduct-for-Research-Integrity-2017.pdf

Seven reasons to Care about Integrity in Research
Science Europe
http://www.scienceeurope.org/wp-content/uploads/2015/06/20150617_Seven-Reasons_web2_Final.pdf

Singapore Statement (http://www.singaporestatement.org) on Research Integrity

Authorship in scientific publications
Swiss Academies of Science
http://www.akademien-schweiz.ch/dms/D/Publikationen/Richtlinien_Empfehlungen/Wiss_Integritaet/Akademien_Autorschaft.pdf

ENRIO – European Network for Research Integrity Officers
http://www.enrio.eu

WCRIF – World Conference on Research Integrity Foundation
http://www.wcri2017.org

Ombudsman für die Wissenschaft
http://www.ombudsman-fuer-die-wissenschaft.de

Thank you.

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