F3
2020

Fighting Fake Facts

3 Februar 2020, Basel, Schweiz

Welcome

Prof. Torsten Schwede
Vizerektor Forschung, Universität Basel

University of Basel

Grigori Alexandrowitsch Potjomkin
Von Johann Baptist von Lampi - Eremitage


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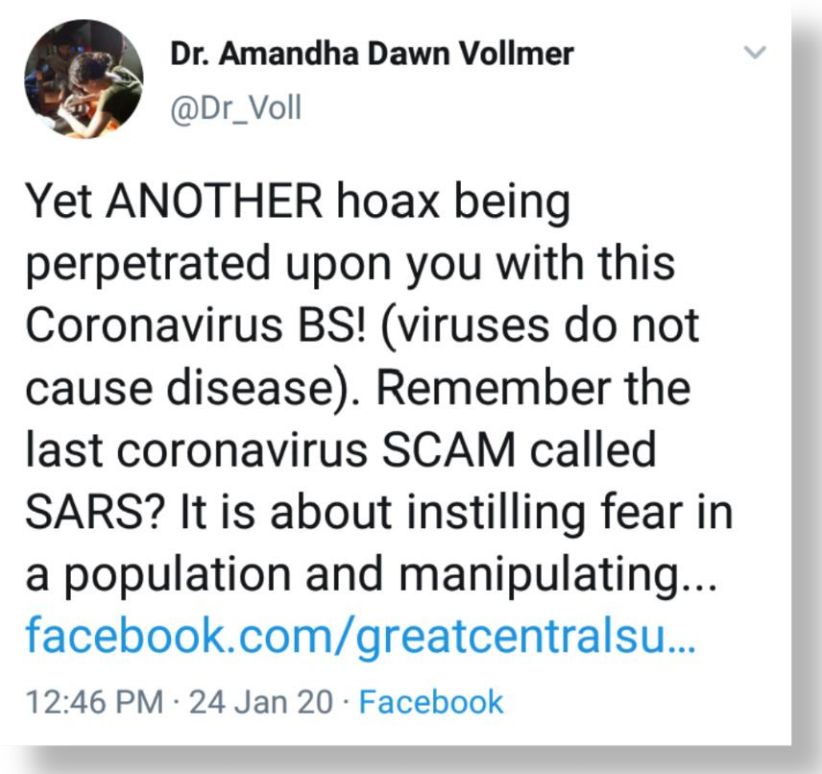
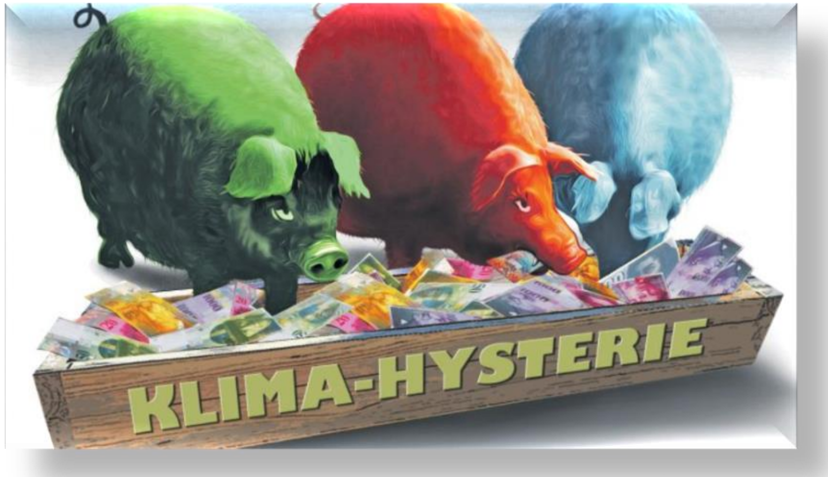


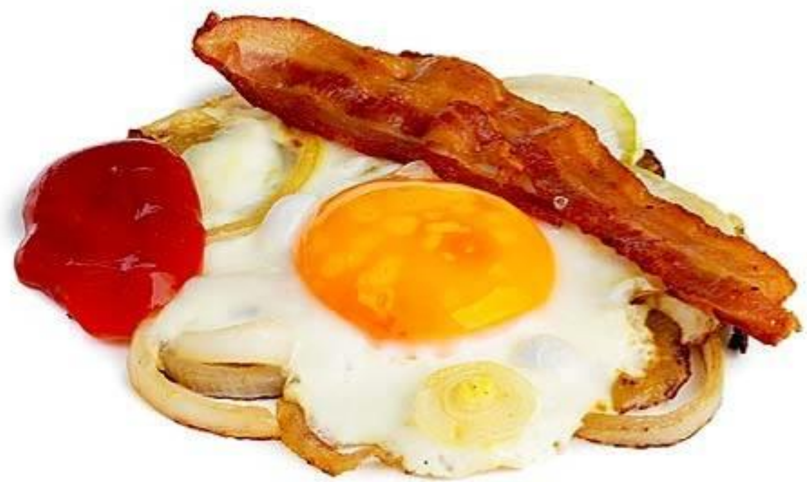
Dr. Amandha Dawn Vollmer
@Dr_Voll

Yet ANOTHER hoax being perpetrated upon you with this Coronavirus BS! (viruses do not cause disease). Remember the last coronavirus SCAM called SARS? It is about instilling fear in a population and manipulating... facebook.com/greatcentralsu…

12:46 PM · 24 Jan 20 · Facebook



Gleiches "Genom" – aber dennoch nicht “gleich”?



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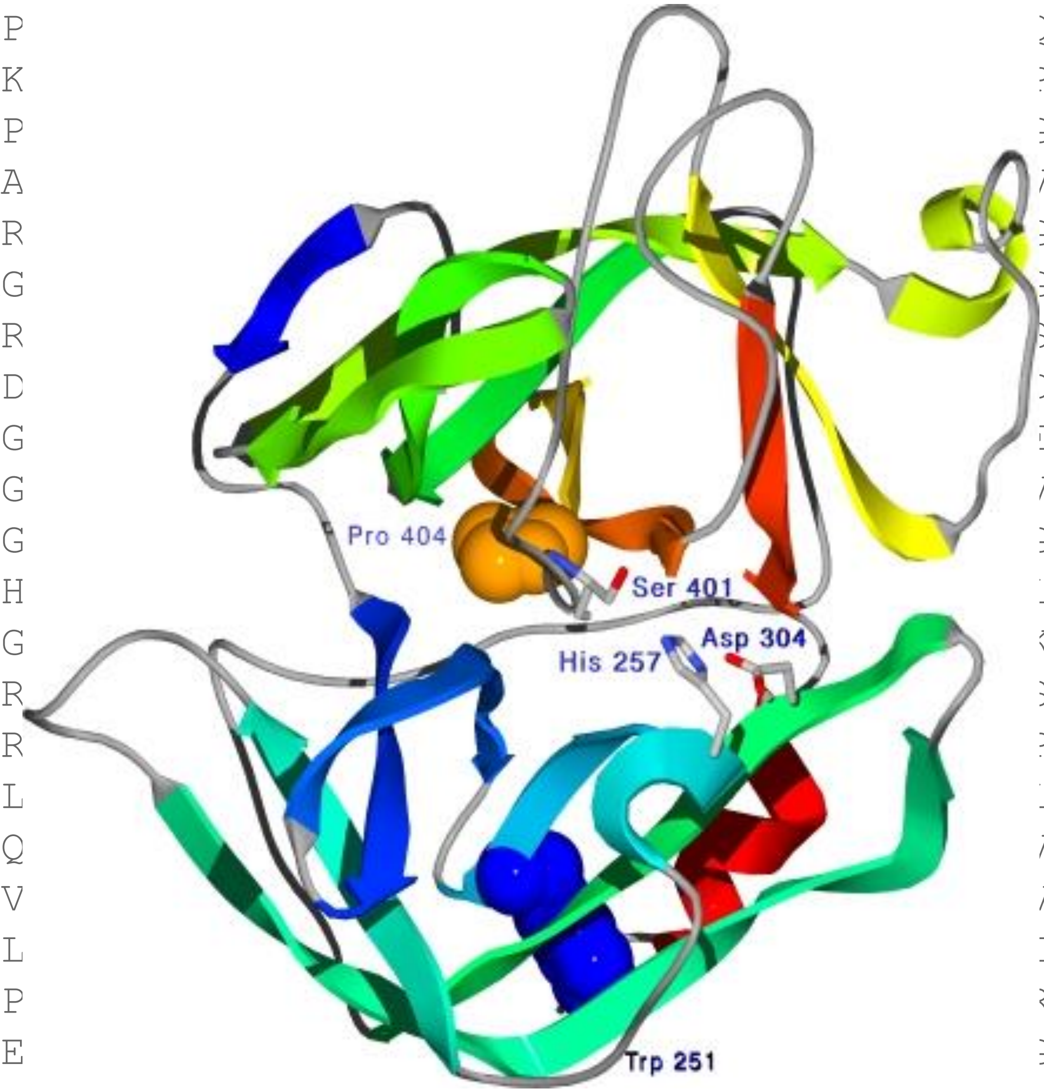

QASGLNVVML GMAGADPEQL RRLAP PRPEPCPVY CPKGQKGEPG EMGLRGQVGP
PGDPGLPGRT GAPGPQGPPG SATAK GPRGDPGER GPRGPKGEPG APGQVIGGEG
PGLPGRKGDP GPSGPPGPRG PLGDP EPGLPGLPG SPGPQGPVGP PGKKGEKGDS
EDGAPGLPGQ PGSPGEQGPR GPPGA AGRPGAKGP EGPPGPTGRQ GEKGEPGRPG
DPAVVGPAVA GPKGEKGDVG PAGPR RAGPPGDSG PPGEKGDPGR PGPPGPVGPR
GRDGEVGEKG DEGPPGDPGL PGKAG PKGDRGEPG PPGPPGRLVD TGPGAREKGE
PGDRGQEGPR GPKGDPGLPG APGER GLDGKPGAA GPSGPNGAAG KAGDPGRDGL
PGLRGEQGLP GPSGPPGLPG KPGED GPKGERGAP GILGPQGPPG LPGPVGPPGQ
GFPGVPGGTG PKGDRGETGS KGEQG TWDESSGSF LPVPERRRGP KGDSGEQGPP
GKEGPIGFPG ERGLKGDRGD PGPQG GEAGRPGER GERGEKGERG EQGRDGPPGL
PGTPGPPGPP GPKVSVDEPG PGLSG EPGPRGQDG NPGLPGERGM AGPEGKPGLQ
GPRGPPGPVG GHGDPGPPGA VRAQH EGLVLPFSG AASAQGVRFA TVQYSDDPRT
EFGLDALGSG GDVIRAIREL SYKGG SQDLVDTAA QRLKGQGVKL FAVGIKNADP
EELKRVASQP TSDFFFFVND FSILR EPSSQSLRV QWTAASGPVT GYKVQYTPLT
GLGQPLPSER QEVNVPAGET SVRLR ELTIQNTTA HSLLVAWRSV PGATGYRVTW
RVLSGGPTQQ QELGPGQGSV LLRDL RPVILGPTS ILLSWNLVPE ARGYRLEWRR
ETGLEPPQKV VLPSDVTRYQ LDGLQ TDLQATELP GQRVRVSWSP VPGATQYRII
VRSTQGVERT LVLPGSQTAF DLDDV PGLRVVVSD ATRVRVAWGP VPGASGFRIS
WSTGSGPESS QTLPPDSTAT DITGL VHVTQASSS SVTITWTRVP GATGYRVSWH
SAHGPEKSQL VSGEATVAEL DGLEP LQILNASSD VLRITWVGVT GATAYRLAWG
RSEGGPMRHQ ILPGNTDSAE IRGLE TLHVVQRGE HSLRLRWEPV PRAQGFLLHW
QPEGGQEQSR VLGPELSSYH LDGLEPATQY RVRLSVLGPA GEGPSAEVTA RTESPRVPSI ELRVVDTSID SVTLAWTPVS RASSYILSWR
PLRGPGQEVP

Proteine besitzen eine charakteristische 3-dimensionale Struktur,
die für ihre Funktion verantwortlich ist.

Von der Sequenz zur Proteinstruktur:

```
MGENDPPAVEAPFSFRSLFGLDDLKISPVAPDA
DAVAAQILSLLPLKFFPIIVIGIIALILALAIG
LGIHFDCSGKYRCRSSFKCIELIARCDGVSDCK
DGEDEYRCVRVGGQNAVLQVFTAASWKTMCSDD
WKGHYANVACAQLGFPSYVSSDNLRVSSLEGQF
REEFVSIDHLLPDDKVTALHHSVYVREGCASGH
VVTLQCTACGHRRGYSSRIVGGNMSLLSQWPWQ
ASLQFQGYHLCGGSVITPLWIITAAHCVYDLYL
PKSWTIQVGLVSLLDNPAPSHLVEKIVYHSKYK
PKRLGNDIALMKLAGPLTFNEMIQPVCLPNSEE
NFPDGKVCWTSGWGATEDGAGDASPVLNHAAVP
LISNKICNHRDVYGGIISPSMLCAGYLTGGVDS
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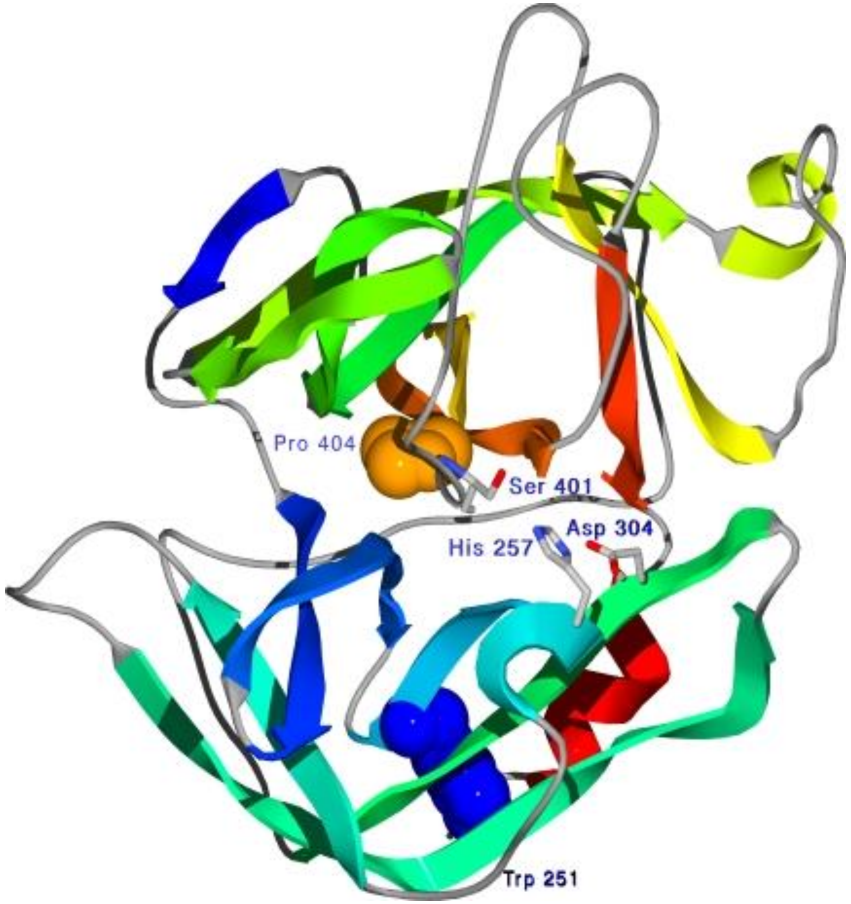
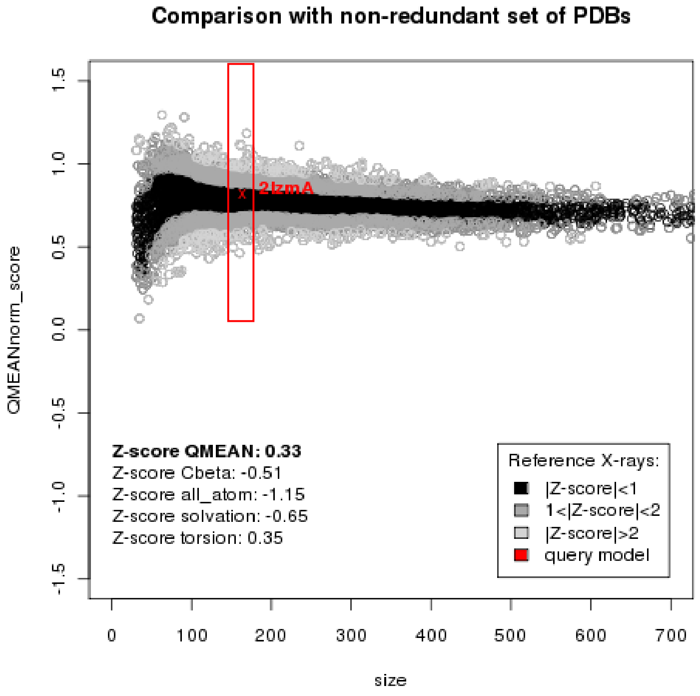


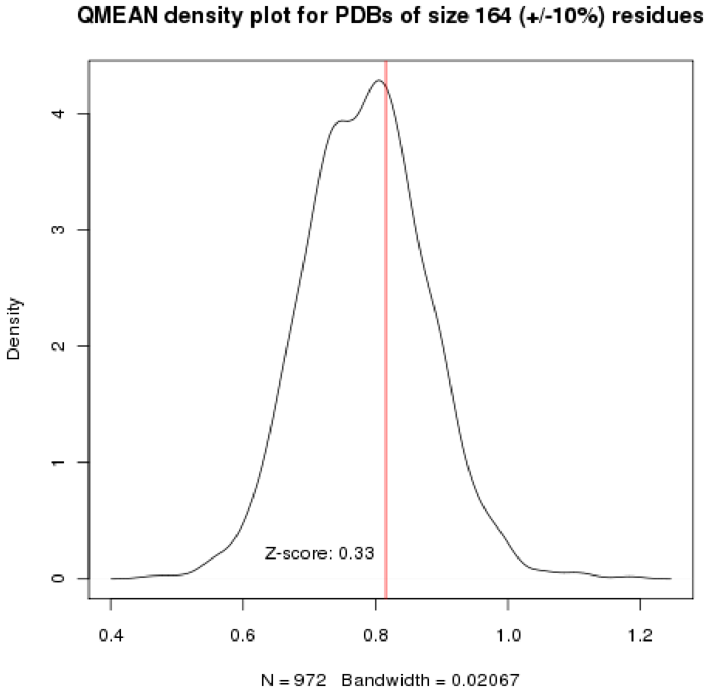
Magritte,
La Clairevoyance,
1936

Wie realitisch sind Homologiemodelle?

- Statitischer Vergleich mit experimentellen Strukturen ähnlicher Grösse

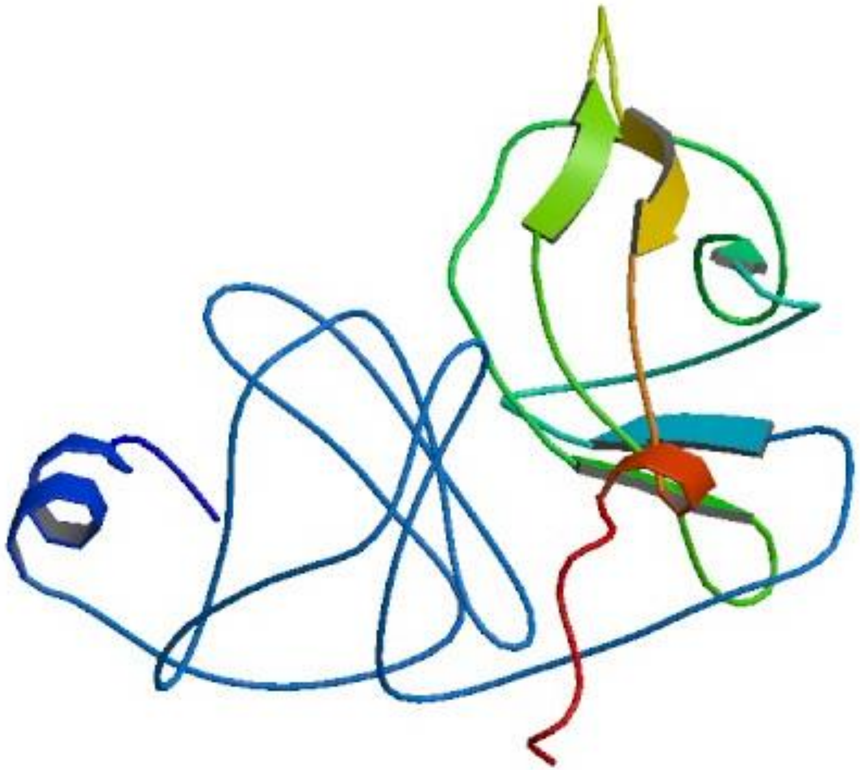
Example:
T4 lysozyme
(2lzm)

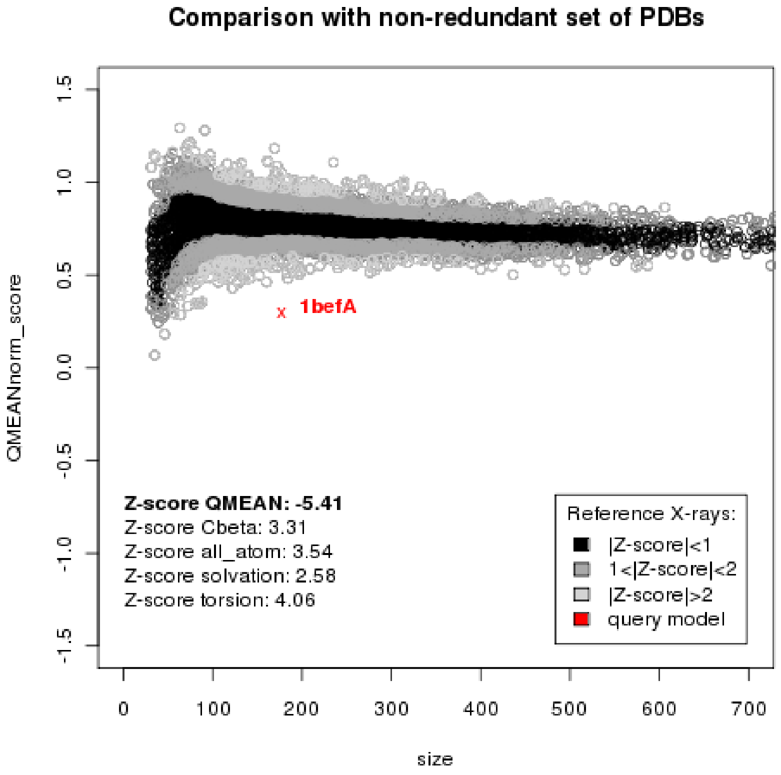




(Benkert, P., Biasini, M. and Schwede, T. (2010). Bioinformatics, 27(3), 343–350.)

1BEF: Dengue Virus NS3 Serine Protease.





HM Murthy, S Clum, R Padmanabhan
J.Biol.Chem. (1999) 274: 5573 - 5580

Res = 2.1 Å; R (R_{free}) 0.186 (0.228)

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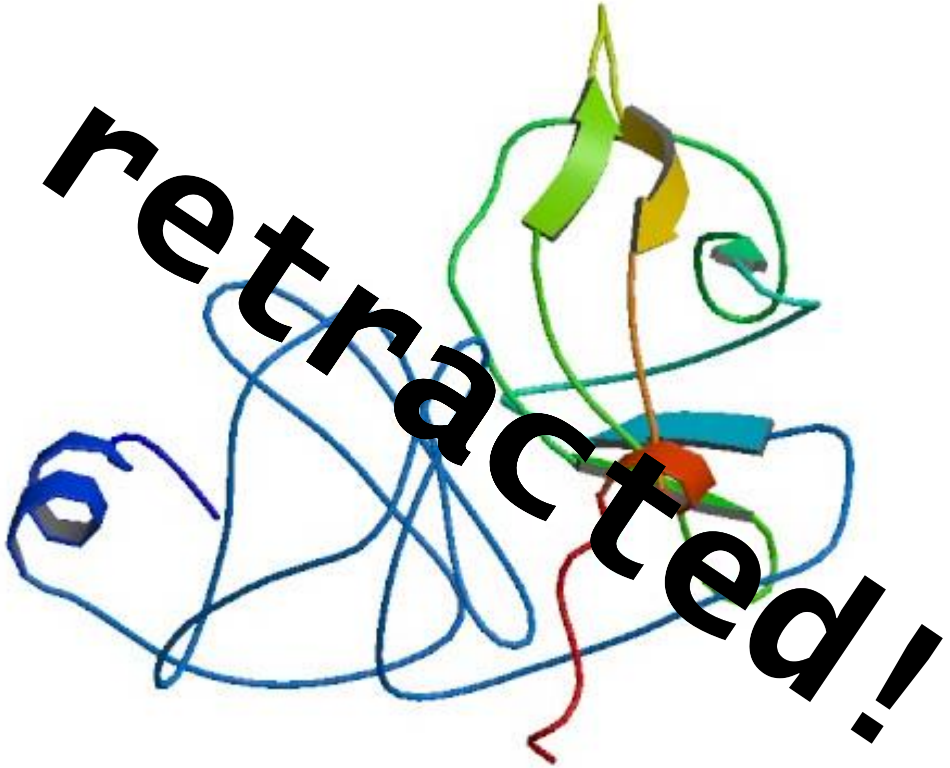

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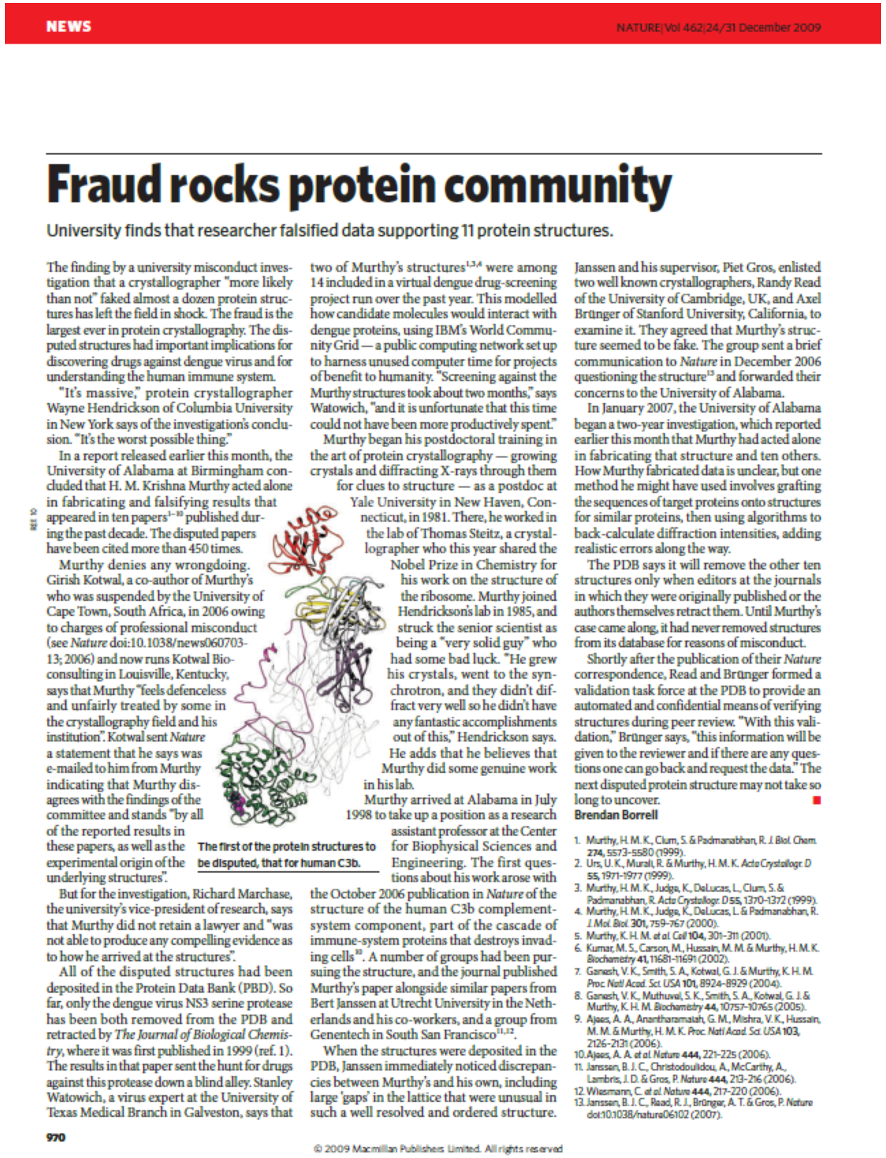

NEWS NATURE|Vol 462|24/31 December 2009

Fraud rocks protein community

University finds that researcher falsified data supporting 11 protein structures.

The finding by a university misconduct investigation that a crystallographer "more likely than not" faked almost a dozen protein structures has left the field in shock. The fraud is the largest ever in protein crystallography. The disputed structures had important implications for discovering drugs against dengue virus and for understanding the human immune system.

"It's massive," protein crystallographer Wayne Hendrickson of Columbia University in New York says of the investigation's conclusion. "It's the worst possible thing."

In a report released earlier this month, the University of Alabama at Birmingham concluded that H. M. Krishna Murthy acted alone in fabricating and falsifying results that appeared in ten papers[1–10] published during the past decade. The disputed papers have been cited more than 450 times.

Murthy denies any wrongdoing. Girish Kotwal, a co-author of Murthy's who was suspended by the University of Cape Town, South Africa, in 2006 owing to charges of professional misconduct (see *Nature* doi:10.1038/news060703-13; 2006) and now runs Kotwal Bioconsulting in Louisville, Kentucky, says that Murthy "feels defenceless and unfairly treated by some in the crystallography field and his institution". Kotwal sent *Nature* a statement that he says was e-mailed to him from Murthy indicating that Murthy disagrees with the findings of the committee and stands "by all of the reported results in these papers, as well as the experimental origin of the underlying structures".

But for the investigation, Richard Marchase, the university's vice-president of research, says that Murthy did not retain a lawyer and "was not able to produce any compelling evidence as to how he arrived at the structures".

All of the disputed structures had been deposited in the Protein Data Bank (PBD). So far, only the dengue virus NS3 serine protease has been both removed from the PDB and retracted by *The Journal of Biological Chemistry*, where it was first published in 1999 (ref. 1). The results in that paper sent the hunt for drugs against this protease down a blind alley. Stanley Watowich, a virus expert at the University of Texas Medical Branch in Galveston, says that two of Murthy's structures[1,3,4] were among 14 included in a virtual dengue drug-screening project run over the past year. This modelled how candidate molecules would interact with dengue proteins, using IBM's World Community Grid — a public computing network set up to harness unused computer time for projects of benefit to humanity. "Screening against the Murthy structures took about two months," says Watowich, "and it is unfortunate that this time could not have been more productively spent."

Murthy began his postdoctoral training in the art of protein crystallography — growing crystals and diffracting X-rays through them for clues to structure — as a postdoc at Yale University in New Haven, Connecticut, in 1981. There, he worked in the lab of Thomas Steitz, a crystallographer who this year shared the Nobel Prize in Chemistry for his work on the structure of the ribosome. Murthy joined Hendrickson's lab in 1985, and struck the senior scientist as being a "very solid guy" who had some bad luck. "He grew his crystals, went to the synchrotron, and they didn't diffract very well so he didn't have any fantastic accomplishments out of this," Hendrickson says. He adds that he believes that Murthy did some genuine work in his lab.

The first of the protein structures to be disputed, that for human C3b.

Murthy arrived at Alabama in July 1998 to take up a position as a research assistant professor at the Center for Biophysical Sciences and Engineering. The first questions about his work arose with the October 2006 publication in *Nature* of the structure of the human C3b complement-system component, part of the cascade of immune-system proteins that destroys invading cells[10]. A number of groups had been pursuing the structure, and the journal published Murthy's paper alongside similar papers from Bert Janssen at Utrecht University in the Netherlands and his co-workers, and a group from Genentech in South San Francisco[11,12].

When the structures were deposited in the PDB, Janssen immediately noticed discrepancies between Murthy's and his own, including large 'gaps' in the lattice that were unusual in such a well resolved and ordered structure. Janssen and his supervisor, Piet Gros, enlisted two well known crystallographers, Randy Read of the University of Cambridge, UK, and Axel Brünger of Stanford University, California, to examine it. They agreed that Murthy's structure seemed to be fake. The group sent a brief communication to *Nature* in December 2006 questioning the structure[13] and forwarded their concerns to the University of Alabama.

In January 2007, the University of Alabama began a two-year investigation, which reported earlier this month that Murthy had acted alone in fabricating that structure and ten others. How Murthy fabricated data is unclear, but one method he might have used involves grafting the sequences of target proteins onto structures for similar proteins, then using algorithms to back-calculate diffraction intensities, adding realistic errors along the way.

The PDB says it will remove the other ten structures only when editors at the journals in which they were originally published or the authors themselves retract them. Until Murthy's case came along, it had never removed structures from its database for reasons of misconduct.

Shortly after the publication of their *Nature* correspondence, Read and Brünger formed a validation task force at the PDB to provide an automated and confidential means of verifying structures during peer review. "With this validation," Brünger says, "this information will be given to the reviewer and if there are any questions one can go back and request the data." The next disputed protein structure may not take so long to uncover. ■

Brendan Borrell

1. Murthy, H. M. K., Clum, S. & Padmanabhan, R. *J. Biol. Chem.* **274**, 5573–5580 (1999).
2. Urs, U. K., Murali, R. & Murthy, H. M. K. *Acta Crystallogr. D* **55**, 1971–1977 (1999).
3. Murthy, H. M. K., Judge, K., DeLucas, L., Clum, S. & Padmanabhan, R. *Acta Crystallogr. D* **55**, 1370–1372 (1999).
4. Murthy, H. M. K., Judge, K., DeLucas, L. & Padmanabhan, R. *J. Mol. Biol.* **301**, 759–767 (2000).
5. Murthy, K. H. M. *et al. Cell* **104**, 301–311 (2001).
6. Kumar, M. S., Carson, M., Hussain, M. M. & Murthy, H. M. K. *Biochemistry* **41**, 11681–11691 (2002).
7. Ganesh, V. K., Smith, S. A., Kotwal, G. J. & Murthy, K. H. M. *Proc. Natl Acad. Sci. USA* **101**, 8924–8929 (2004).
8. Ganesh, V. K., Muthuvel, S. K., Smith, S. A., Kotwal, G. J. & Murthy, K. H. M. *Biochemistry* **44**, 10757–10765 (2005).
9. Ajees, A. A., Anantharamaiah, G. M., Mishra, V. K., Hussain, M. M. & Murthy, H. M. K. *Proc. Natl Acad. Sci. USA* **103**, 2126–2131 (2006).
10. Ajees, A. A. *et al. Nature* **444**, 221–225 (2006).
11. Janssen, B. J. C., Christodoulidou, A., McCarthy, A., Lambris, J. D. & Gros, P. *Nature* **444**, 213–216 (2006).
12. Wiesmann, C. *et al. Nature* **444**, 217–220 (2006).
13. Janssen, B. J. C., Read, R. J., Brünger, A. T. & Gros, P. *Nature* doi:10.1038/nature06102 (2007).

http://www.snf.ch/de/fokusForschung/themendossiers/open-science/Seiten/default.aspx

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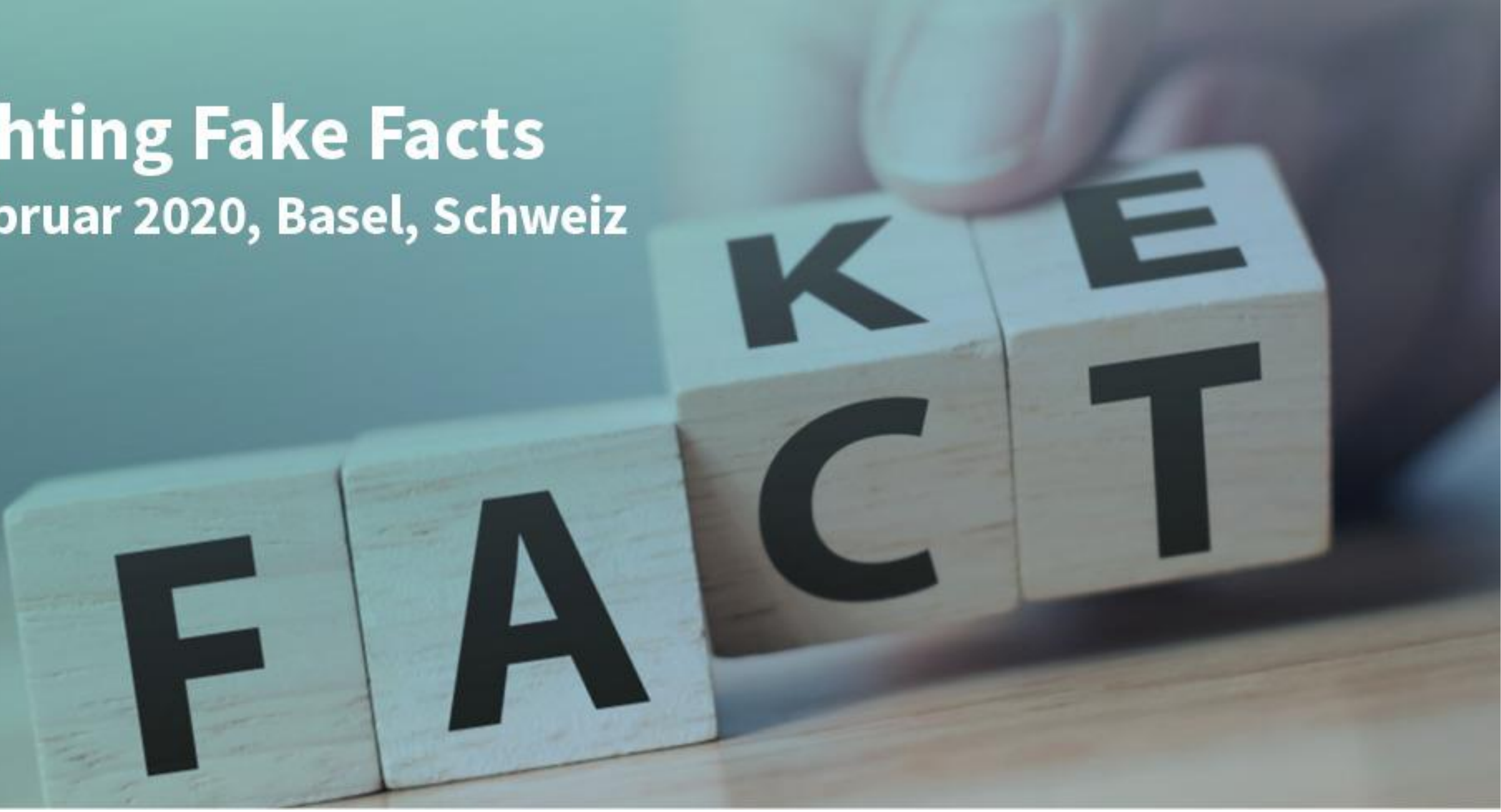

Welcome

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