ENSSER Statement on Séralini et al. (2012) publication and reactions evoked

Questionable Biosafety of GMOs, Double Standards and, once again, a "Shooting-the-Messenger" style Debate

Summary and Main Issues

The European Network of Scientists for Social and Environmental Responsibility (ENSSER) welcomes the study "Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize" by a group of research scientists of the French Committee for Research and Independent Information on Genetic Engineering (CRIIGEN), an institutional member of ENSSER. Séralini et al. (2012) report on a two-year, full life-cycle study with rats testing Monsanto's NK603 glyphosate-tolerant GM maize (single trait glyphosate tolerance) and its Roundup co-technology in the journal *Food and Chemical Toxicology*.

The group of researchers led by Prof. Séralini has published previous toxicology studies on Roundup and its active ingredient glyphosate (Gasnier et al. 2009; Benachour et al. 2007; Benachour & Séralini 2009). The scientists also evaluated historical industry data. These data from feeding trials with rats were submitted in support of the company's dossers seeking approval for food/feed import. When re-analysing the developer's raw data, they found signs for toxicological effects on rat liver and kidneys after 90 days of feeding with GM maize, including the GM maize NK603 tested in this new study (de Vendômois et al. 2009; Séralini et al. 2007; Séralini et al. 2011).

Repeated calls that regulators should require more rigorous, long-term follow-up studies by the developers have consistently been ignored or rejected on dubious grounds. In 2011, the European Food Safety Authority (EFSA) still rejected *mandatory* 90-day feeding studies as a requirement for applications for GM food and feed (European Food Safety Authority 2011). The few studies that were carried out by developers are voluntary and apply protocols of their choosing.

Main issues

1. CRIIGEN's research[1] was crucial in finally eliciting a policy response by the European competent authority, the European Commission's Directorate-General SANCO (Health and Consumer Safety) in 2012. In its draft Implementing Regulation on applications for authorisation of genetically modified food and feed (European Commission 2012), the European Commission stated: "toxicological studies with the whole genetically modified food and feed shall be carried out." If adopted, applicants "shall include a 90-day feeding study with whole food and feed in rodents for the assessment of food and feed containing, consisting of or produced from genetically modified plants [...]."
2. After a careful comparative analysis of both industry published data and that of CRIIGEN, ENSSER concludes that most arguments which attempt to invalidate the Séralini et al. study cannot hold up to closer scrutiny. Raised criticisms are to a large extent either wrong or apply double standards. The weak point of the pilot study by Séralini et al. is the

[1] GMO RISK EVALUATION - A Contradictory Debate, Parliamentary Workshop 2011
http://www.ensser.org/developing-responsible-approaches-to-risk-assessment/aldeeu-parliament-workshop-2011-brussels/

number of animals used, which does not allow a statistical analysis of the raw data regarding one parameter measured out of over 30 - mortality. This has been acknowledged by the authors and needs to be considered/remediated in follow-up studies.

3. The controversy and vitriolic attacks evoked by the study reveal one underlying aspect: The lack of appropriate and agreed methodologies for long-term studies to scientifically assess effects of the life-time consumption of GM foods.
4. The development of such methodology and tests, which have been demanded by concerned scientists ever since GM food was announced to be introduced into the international markets, has systematically been blocked by lobby work of industry and associated scientists. International bodies such as the Codex Alimentarius and national governments - including most EU governments and their authorities - accepted instead the concept of substantial equivalence and the concept of familiarity to evade any scientific mandatory testing of GM food for human health safety and to simply declare significant differences found between GMOs and their unmodified parents as 'biologically irrelevant' in an assumption-based approach.
5. The acceptance of these industry-led constructed models providing the conceptual justification for evading testing of food-related risks associated with the introduction of this new technology and neglecting the clearly formulated demands of European citizens led to the crisis of trust in science & regulations that now come to light with full force.
6. Due to the proven close links between industry and EU risk assessors and the documented disproportional influence on regulations by developers and owners of the technology, it is predictable and expected that these authorities, including EFSA, will not be able to substantially revise their original assessment of GM maize NK603 (and any other application) as their credibility is at stake. This is highlighted for example by the European Parliament (2012) refusing the discharge of the EFSA 2010 budget as long as there is no fundamental change in policy, leadership and guidance.

1 Immediate Responses and Attacks

The publication of this study triggered orchestrated discrediting campaigns against the authors and their work, similar to previous campaigns attempting to discredit other studies finding adverse effects. This strategy has been analysed over many years and extensively described for example in the journal Nature (Waltz 2009) and Hilbeck et al. (2012). While it therefore comes as no surprise, it should be decried as contrary to sound scientific principles, and thus institutional anti-science. ENSSER condemns all *ad hominem* attacks and arguments and the emotional, often vicious conduct of the debate, like for example those that have gone on record in a recent article on this issue by John Vidal (2012) in the Guardian. Further examples are the press release by the Council for Biotechnology Information (CBI 2012) of the U.S. biotechnology industry and the business magazine Forbes (Miller & Chassy 2012) featuring public sector scientists and a retired regulator with a long personal record of rejecting the U.N. Cartagena Protocol on Biosafety of specific GMO legislation. Miller & Chassy (2012) attack the numerous peer-reviewed publications by CRIIGEN researchers in well-respected international scientific journals: "Séralini has made a specialty of methodologically flawed, irrelevant, uninterpretable - but over-interpreted - experiments intended to demonstrate harm from genetically engineered plants and the herbicide glyphosate in various highly contrived scenarios". For those interested in reading more, we refer to the original articles for the reader to decide whether this style meets their standards.

2 Methodology and results of the Séralini et al. study

In 2010, CRIIGEN acquired external funding and set up this study to further explore the signs of toxicity observed in the experimental data delivered by Monsanto Company. Hence, a toxicology trial was designed with the standard 10 rats per sex (total 20 for both sexes), as recommended by the revised OECD Guidelines 408 (Organisation for Economic Cooperation and Development 1998). The authors did not apply the OECD Guidelines 451 (Carcinogenicity Studies) or 453 (Combined Chronic Toxicity\Carcinogenicity Studies) - as demanded by commentators - because the authors did not intend to conduct carcinogenicity studies in the first place. It was their intent to apply the Guideline 408 methodology in an extended time span.

2.1 Critique of scientific aspects

The most often repeated arguments by critics of Séralini et al are so far:

2.1.1 The use of Sprague Dawley rats that are prone to high natural background cancer-rates

These rats are used routinely in such studies for toxicological and tumour inducing effects, including those by Monsanto as basis for the approval of NK603 maize and other GM crops (Hammond et al., 1996, 2004, 2006; MacKenzie et al., 2007). Most critical commentators of the Séralini et al. study failed to inform their readership about this fact. Séralini at al. used this rat strain to keep their study design as comparable to Monsanto's as possible. Had they used another rat strain and shown adverse effects, the relevance of their results probably would have been challenged on that basis, i.e. the use of different types of rats.

Contrary to the broad claims of commentators, Sprague Dawley rats are also frequently used in long-term toxicity/carcinogenicity studies.

1. The National Toxicology Program of the U.S. Department of Health and Human Services[2] uses this strain in its 2-year studies, uncontested.
2. A brief, quick and still preliminary literature search of peer-reviewed journals revealed that Sprague Dawley rats were used
   - in 36-month studies by Voss et al. (2005);
   - in 24-month studies by Hack et al. (1995), Klimisch et al. (1997), Minardi et al. (2002), Soffritti et al. (2006) and Gaméz et al. (2007);
   - in 18-month studies by Lee et al. (2010); and
   - in 12-month studies by Perry et al. (1981), Conti et al. (1988), Morcos & Camilo (2001), Flamm et al. (2003) and Gutiérrez et al. (2011).

Four of these studies had been published in *Food and Chemical Toxicology*.

2.1.2 Food uptake not quantified

Food was offered *ad libidum* in the Séralini et al. rat studies, as is also often done, for example in the above-mentioned industry studies serving as the basis for GM crop approvals. Hammond et al. (2006) - the Monsanto feeding study for approval of NK603 - also did not measure daily food-intake during the trial to establish the amount of toxins ingested. In addition, Monsanto's Technical dossiers assessed by EFSA for food and feed approval of GM

[2] http://ntp.niehs.nih.gov/?objectid=72015DAF-BDB7-CEBA-F9A7F9CAA57DD7F5

maize MON88017 and MON89034 both state "Each diet was presented ad libitum for approximately 90 days to 20 male and 20 female Sprague-Dawley [Crl:CD®24 (SD)] rats of approximately 6-8 weeks of age at study initiation. During the study, animals were observed twice daily for mortality and moribundity. Detailed physical examinations, including behavioural observations outside the home cage, individual body weights and food consumption were recorded weekly." This approach was accepted by EFSA and did not evoke comments by those criticising the same approach as used by Séralini at al.. Furthermore, Monsanto conducted clinical pathology evaluations on only 10 of the above mentioned 20 treated rats, the criteria for selection remained undisclosed in the Technical Dossier.

We would like to underline: the lack of quantification of the amount of toxin ingested does by no means invalidate the observed clinical symptoms. We would like to underline: the lack of quantification of the amount of toxin ingested does by no means invalidate the observed clinical symptoms. This might be a problem for a negative result, where no toxic effects were seen, but is not a concern for a positive result

2.1.3 Sample size too small for a long-term trial

The sample size is appropriate for 90-day toxicology trials, but insufficient for proof of long-term toxicity/carcinogenicity studies. The authors acknowledge that and, therefore, present the raw data on mortality and tumour development for each individual, which are indicative for tumour forming. One possible remediation could be that the authors evaluate their data for 3-4 months toxicity effects only and separate them from those observed afterwards.

3 Critique of disclosure policy and funding sources

Critical commentators have demanded the full disclosure of the raw data and pointed to the GM-critical stance of the financial source organisations that would provide incentives to design experimental set-ups that are more likely to detect negative outcomes. CRIIGEN announced its willingness to disclose data in the context of a fair and independent review. Again, the many calls for full disclosure as for example posted at an internet petition (Prakash et al. 2012) reveal familiar double standards. None of those experts - many of them with a long documented record of rejecting the basic principles of the EU biosafety legislation and opposing the improvement of risk assessment standards to meet these principles - was heard during the time when data related to the applications for release and marketing of GM crops were kept secret by the regulator upon demand of the applicants and some of which could only be obtained by court decision.

Following the logic of the funding argument, which is distinct from the unrestricted disclosure point, it can be stated that it is the developers – obviously (and in principle, legitimately) pro-GM sources - which fund all regulatory trials. These are thus prone to embody methodologies or discretionary technical judgements and assumptions that will find no adverse effects. The application of this logic would invalidate all studies funded or conducted by industry and accepted by risk assessors and regulators. Clearly industrial promoters must be involved in risk assessment studies; but others funded indirectly by those interests, but not influenced directly or indirectly by them, have to be free to perform fully independent risk assessments. This will require new institutional and perhaps legislative arrangements in regulation and science funding, and this focused debate urgently needs to be initiated, by the responsible public authorities.

4 Double standards and asymmetric scrutiny

A factual comparative analysis of the rat feeding trial by the Séralini group and the Monsanto trials clearly reveals that if the Séralini experiments are considered to be insufficient to demonstrate harm, logically, so must be those carried out by Monsanto to prove safety.

Basically, all previous studies finding adverse effects of GE crops have been treated by regulators with: only those studies showing adverse effects receive a rigorous evaluation of their experimental and statistical methods, while those that claim proof of safety are taken at face value (e.g. see also Hilbeck et al. 2012). This asymmetric scrutiny is applied by EFSA on a regular basis as confirmed in an interview with a former EFSA GMO panel member who stated: 'Of course, studies that describe potential negative environmental effects of GMOs are discussed particularly intensively' (Anonymus 2009). According to Millstone et al. (2004), this practice is interpreted by the European public as an illegitimate support for the biotechnology industry, by the supposedly impartial risk assessor. They state that 'greater institutional care was taken to try to avoid false positives than to avoid false negatives. That implies that critical scrutiny has been applied in an asymmetrical fashion that prima facie seems difficult to reconcile with a precautionary approach'.

A recent review by Snell et al. (2012) illustrates this same issue. In the abstract, the authors state "Results from all the 24 studies [reviewed] do not suggest any health hazards [...]" - taking all those studies at face value. Yet in their review, the authors find numerous weaknesses of similar or greater severity as raised for the Séralini group's paper. For example, of the 24 studies they evaluated 16 (67% of all studies) did not mention using the isogenic line as control (interpreted as having not used them), many did not describe the methods in any detail, used lower numbers of animals than Séralini et al, and according to the reviewers had other deficiencies too. All studies reported no adverse effects and were accepted as proof of safety regardless of these manifest (but deemed irrelevant) deficiencies of their methods.

ENSSER calls for an end to these double standards and the 'shooting of the messenger' style conduct of the debate!

If the Séralini et al. study is found to be insufficient to prove harm due to methodological failings, then all previous studies submitted in support of approvals for food and feed in the EU must be reconsidered regarding their evidence for safety to human and animal health, and must be scrutinized according with the same level of rigour as is applied to such studies showing adverse effects. Likewise, a call for disclosure of all raw data by Séralini *et al.* must obviously be matched by full disclosure of all the raw data – and crucially also the biological materials at issue - by all applicants. Asymmetrical risk assessments are clearly unacceptable and comply with neither elementary standards of scientific process, nor basic standards of public propriety, nor with the precautionary principle. **The burden of proof should lie clearly on the developer to demonstrate adequate evidence of safety, and not on a public research group, which is not given the necessary data, materials nor resources, to prove harm!** It is difficult to resist describing this state of affairs as scandalous.

ENSSER also calls for a systematic global, comprehensive, in-depth survey and synthesis of all the anecdotal reports on record, dismissed studies, and observations from various sources (farmers, herders, veterinarians, medical staff etc) in various countries that have accumulated over the past 15 years. This survey should include ingestions/application of GM crops and of Roundup/glyphosate (evidence is accumulating that Roundup/glyphosate is far

more toxic than the public and the regulators were made to believe). ENSSER could provide a list of such reports. A careful evaluation of the totality of all reports in search of potential common underlying patterns and, if so, careful evaluation of whether or not these are in agreement with the sparse reported data in the published literature from controlled experiments. A supra-national group of independent researchers / organizations should oversee this comprehensive report. Independence in this case would mean independence from the economic interests of the developers and IPR owners of the respective GE events and plants and of those who have a stake in this debate.

This recommendation is prudent for two reasons:

1. It would be one necessary next step to follow-up on these first data published by the group of Prof Séralini; and
2. This would for the first time since the release of this milestone report, constitute a conscientious implementation of what the collective of authors for the European Environmental Agency (2001), *Late Lessons from Early Warnings*, called for: an inclusive and diverse range of sources of multidisciplinary and experienced practitioners witnessing of possible unexpected adverse effects of such new technologies, often enacted in conditions not foreseen or tested by laboratory conditions. As the EEA volume demonstrated, such a genuinely precautionary approach does not have to imply nor be condemned as obstruction to innovation and benefit from science and technology, indeed it can stimulate new, more responsible, more scientifically informed and more socially beneficial technological trajectories.

Even the very best and most expensive, exhaustive scientific knowledge will never suffice on its own for making responsible decisions on such complex public interest matters as the approval or control of commercially-promoted agricultural innovations. There will always also be normative social and ethical priorities and needs, which need to interrogate as well as be informed by the best available knowledge, and then debated and democratically decided.

ENSSER asserts that existing structures of science and policy for agricultural biotechnology and agricultural innovation and regulation more generally in Europe require an accountable and inclusive process of reappraisal and change. The key purpose of such institutional change would be to remove what are clearly anti-scientific standards and procedures, with a systematically ingrained bias against the conditions for sound independent science, and thus against soundly-informed as well as legitimately-decided public policy. In regulation and risk assessment of GM crops, egregious and blatant inconsistencies of institutional behaviour with the normative standards of sound science, which are declared and claimed for themselves by those same institutions, not only discredit science in the public arena, but discredit EU policy, and EU policy and scientific advisory institutions, too. Such change is possible – and urgent.

References

Anonymus (2009) EFSA: New Members for GMO Panel. GMO Biosafety, 10.06.2009 http://www.gmo-safety.eu/news/622.efsamembers-gmo-panel.html

Benachour N, G E Séralini (2009) Glyphosate Formulations Induce Apoptosis and Necrosis in Human Umbilical, Embryonic, and Placental Cells. Chemical Research in Toxicology 22: 97-105

Benachour N, H Sipahutar, S Moslerni, C Gasnier, C Travert, G E Séralini (2007) Time- and dose-dependent effects of roundup on human embryonic and placental cells. Archives of Environmental Contamination and Toxicology 53: 126-33

Conti B, C Maltoni, G Perino, A Ciliberti (1988) Long-term carcinogenicity bioassays on styrene administered by inhalation, ingestion and injection and styrene oxide administered by ingestion in Sprague-Dawley rats, and para-methylstyrene administered by ingestion in Sprague-Dawley rats and Swiss mice. Annals of the New York Academy of Sciences 534: 203-34

Council for Biotechnology Information (2012) Scientists in U.S. reject heavily publicized rat study. Press Release, 20.09.2012 http://www.whybiotech.com/newsandevents/release_092012.asp

de Vendômois J S, F Roullier, C Cellier, G E Séralini (2009) A Comparison of the Effects of Three Gm Corn on Mammalian Health. International Journal of Biological Sciences 5: 706-21

European Commission (2012) COMMISSION IMPLEMENTING REGULATION (EU) No …/.. of XXX on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Regulations (EC) No 641/2004 and (EC) No 1981/2006. SANCO/12462/2011 Rev. 1

European Environmental Agency (2001) Late lessons from early warnings: the precautionary principle 1896-2000. Environmental issue report No. 22

European Food Safety Authority (2011) Guidance for risk assessment of food and feed from genetically modified plants. EFSA Journal 9 (5): 2150

European Parliament (2012) Report on discharge in respect of the implementation of the budget of the European Food Safety Authority for the financial year 2010 (C7-0286/2011 – 2011/2226(DEC)), Committee on Budgetary Control, A7-0106/2012

Ewen S W B, A Pusztai (1999) Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. The Lancet 354 (9187): 1353-4

Flamm W G, G L Blackburn, C P Comer, D A Mayhew, W W Stargel (2003) Long-term food consumption and body weight changes in neotame safety studies are consistent with the allometric relationship observed for other sweeteners and during dietary restrictions. Regulatory and Toxicological Pharmacology 38(2): 144-56

Gámez, R, M Noa, R Mas, N Mendoza, B Pardo, R Menéndez, Y Pérez, R M González, A Gutiérrez, G Marrero, E Goicochea, H García, D Curveco (2007) Long-term carcinogenicity of D-003, a mixture of high molecular weight acids from sugarcane wax, in Sprague Dawley rats: A 24 months study. Food and Chemical Toxicology 45 (12): 2352-58

Gasnier C, C Dumont, N Benachour, E Clair, M C Chagnon, G E Séralini (2009) Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. Toxicology 262: 184-91

Gutiérrez A, R Gámez, M Noa, R Mas, D Arencibia, B Pardo, M Valle, A Oyarzábal, D Curveco, H García, E Goicochea, N Mendoza, S Jiménez S (2011) One year oral Toxicity of D-004, a lipid extract from Roystonea regia fruits, in Sprague Dawley rats. Food and Chemical Toxicology 49 (11): 2855-61

Hack R, E Ebert, K H Leist (1995) Chronic toxicity and carcinogenicity studies with the insecticide endosulfan in rats and mice. Food and Chemical Toxicology 33 (11): 941-50.

Hammond B, J L Vicini, C F Hartnell, M W Naylor, C D Knight, E H Robinson, R L Fuchs, S R Padgette (1996) The feeding value of soybeans fed to rats, chickens, catfish and dairy cattle is not altered by genetic incorporation of glyphosate tolerance. Journal of Nutrition 126: 717-272

Hammond B, R Dudek, J Lemen, M Nemeth (2004) Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. Food and Chemical Toxicology 42: 1003–14

Hammond B, R Dudek, J Lemen, M Nemeth (2006) Results of a 90-day safety assurance study with rats fed grain from corn borer-protected corn. Food and Chemical Toxicology 44: 1092–9

Hilbeck A, M Meier, M Trtikova (2012) Underlying reasons of the controversy over adverse effects of Bt toxins on lady beetle and lacewing larvae. Environmental Sciences Europe 24: 9

Klimisch H J, K Deckardt, C Gembardt, B Hildebrand, K Küttler, F J Roe (1997) Long-term inhalation toxicity of N-vinylpyrrolidone-2 vapours. Studies in rats. Food and Chemical Toxicology 35 (10-11): 1041-60

Lee H J, Y M Gimm, H D Choi, N Kim, S H Kim, Y S Lee (2010) Chronic exposure of Sprague-Dawley rats to 20 kHz triangular magnetic fields. International Journal of Radiation Biology 86 (5): 384 - 9

MacKenzie S A, I Lamb, J Schmidt, L Deege, M J Morrisey, M Harper, R J Layton, L M Prochaska, C Sanders, M Locke, J L Mattsson, A Fuentes, B Delaney (2007) Thirteen week feeding study with transgenic maize grain containing event DAS-Ø15Ø7-1 in Sprague–Dawley rats. Food and Chemical Toxicolgy 45: 551–62

Miller H I, B Chassy (2012) Scientists smell a rat in fraudulent genetic engineering study. Forbes, 25.09.2012
http://www.forbes.com/sites/henrymiller/2012/09/25/scientists-smell-a-rat-in-fraudulent-genetic-engineering-study/

Millstone E, P van Zwanenberg, C Marris, L Levidow, H Torgersen (2004) Science in Trade Disputes Related to Potential Risks: Comparative Case Studies. Seville: European Commission

Minardi F, F Belpoggi, M Soffritti, A Ciliberti, M Lauriola, E Cattin, C Maltoni (2002) Results of long-term carcinogenicity bioassay on vinyl acetate monomer in Sprague-Dawley rats. Annals of the New York Academy of Sciences 982: 106-22

Morcos NC, K Camilo (2001) Acute and chronic toxicity study of fish oil and garlic combination. International Journal of Vitamin and Nutrition Research 71(5): 306-12

OECD (1998) OECD Guideline 408. Repeated dose 90-day oral toxicity study in rodents.

Perri G C, A Nunziata, A Argentino-Storino, R O Salerno, P Mercatelli (1981) Long term toxicity and carcinogenicity of a new protein source in rats. Toxicological European Research 3(6): 305-10

Prakash C S et al. (2012) Dr. Seralini - Please release data from your biotech corn study. http://www.ipetitions.com/petition/dr-seralini-please-release-data/

Quist D, I Chapela (2001) Transgenic DNA introgressed into traditional maize landraces in Oaxaca, Mexico. Nature 414 (6863): 541–3

Séralini G E, D Cellier, D, J S de Vendômois (2007) New analysis of a rat feeding study with a genetically modified maize reveals signs of hepatorenal toxicity. Archives of Environmental Contamination and Toxicology 52: 596-602

Séralini G E, E Clair, R Mesnage, S Gress, N Defarge, M Malatesta, D Hennequin, J S du Vendômois (2012) Long term toxicity of a Rondup herbicide and a Roundup-tolerant genetically modified maize. Food and Chemical Toxicology http://dx.doi,org/10.1016/j.fct.2012.08.005.

Séralini G E, R Mesnage, E Clair, S Gress, J S du Vendômois, D Cellier (2011) Genetically modified crops safety assessments: present limits and possible improvements. Environmental Sciences Europe 23: 1-10

Snell C, A Bernheim, J-B Bergé , M Kuntz, G Pascal, A Paris , A E Ricroch (2012) Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: A literature review. Food and Chemical Toxicology 50: 1134–48

Soffritti M, F Belpoggi, D Degli Esposti, L Lambertini (2006) Results of a long-term carcinogenicity bioassay on Sprague-Dawley rats exposed to sodium arsenite administered in drinking water. Annals of the New York Academy of Sciences 1076: 578-91

Vidal J (2012) Study linking GM maize to cancer must be taken seriously by regulators. The Guardian, 28.09.2012 http://www.guardian.co.uk/environment/2012/sep/28/study-gm-maize-cancer

Voss C, H Zerban, P Bannasch, M R Berger (2005) Lifelong exposure to di-(2-ethylhexyl)-phthalate induces tumors in liver and testes of Sprague-Dawley rats. Toxicology 206(3): 359-71

Waltz E (2009) Battlefield. Nature 461: 27 - 32