

Immunology in the spotlight at the Dover ‘Intelligent Design’ trial

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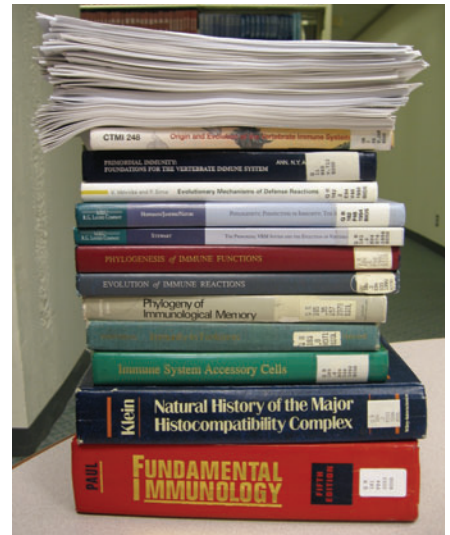
Immunology had an unexpected and decisive part in challenging the claims of ‘Intelligent Design’ proponents at the US trial on the teaching of evolution in public schools in Dover, Pennsylvania.

The latest skirmish in the ongoing controversy about the teaching of evolution in US schools ended decisively on 20 December 2005, when the introduction of ‘Intelligent Design’ (ID) in a public school biology class was struck down by US Federal Judge John E. Jones as an unconstitutional establishment of religion. The case, ‘Kitzmiller *et al.* v. Dover Area School District’, was brought by 11 parents from Dover, Pennsylvania, represented pro bono by the Philadelphia law firm Pepper-Hamilton, together with the American Civil Liberties Union and Americans United for the Separation of Church and State and assisted with scientific support by the National Center for Science Education, the Oakland, California-based nonprofit organization devoted to combating creationism. The parents challenged the school district’s requirement that administrators read to ninth graders a disclaimer raising doubts about evolution, suggesting ID as a better alternative explanation for life’s diversity and referring students to the ID supplemental textbook *Of Pandas and People*, 60 copies of which had been donated to the school library.

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Although the magnitude of the win for science education was a surprise to some, the actual outcome of the trial was in very little doubt, for many reasons. Board members had made clear, through public declarations at board meetings and to the media, their intention to have some form of religious creationism taught in biology classes alongside evolution, which they considered akin to atheism. US Supreme Court rulings have established and repeatedly reaffirmed that governmental policies with the purpose or effect of establishing religion are inadmissible because they violate the First Amendment of the US Constitution. It also did not help their cause that Judge Jones found that some of the board members “either testified inconsistently, or lied outright under oath” about some statements and about the source of the donated *Of Pandas and People* books, the money for which was raised by one of the board members at his own church.

The most important and far-reaching aspect of the decision, however, was that the judge went beyond the narrow issue of the school board’s actions and ruled broadly on the nature of ID and its scientific claims. After a 6-week trial that included extensive expert testimony from both sides on science, philosophy and the history of creationism, Jones ruled that ID is not science but “creationism re-labeled.” Coming from the George W. Bush–appointed, lifelong Republican and church-going Judge Jones, the ruling was all the more stinging for ID advocates and made the predictable charge of ‘judicial activism’ harder to sustain. The ruling is likely to have a substantial effect on many other ongoing cases (and possibly future court decisions) regarding ID and evolution in science curricula from Georgia to Kansas to Ohio.



Evolutionary immunology literature presented at the Dover trial. “We can look high or we can look low, in books or in journals, but the result is the same. The scientific literature has no answers to the question of the origin of the immune system.”²

More fundamentally, the decision represents a considerable setback for ID advocates, who claim that some examples of biological complexity could only have originated by intelligent mechanisms, and for their movement’s now almost-20-year-old effort to gain a foothold in school curricula and project an aura of scientific respectability. The ruling is also of great interest to scientists, not only because of its importance for science education but also because much of the trial’s extensive expert testimony, both for and opposed to ID, focused directly on weighty scientific topics. Judge Jones analyzed and dismissed the core ‘scientific’ assertions of the ID

movement—immunology had an unexpectedly large and relevant part in his reaching those conclusions.

Although the field of evolutionary and comparative immunology has a long and rich history, dating back at least to 1891 (ref. 1), and remains an exciting and rapidly progressing area of research, its direct involvement in the controversies about evolution in schools can be attributed mainly to Michael Behe, professor of biochemistry at Lehigh University (Bethlehem, Pennsylvania), leading ID advocate and star expert witness for the defense at this trial. In his 1996 book *Darwin's Black Box*², a commonly cited example of ID-based 'science', Behe devotes an entire chapter to the immune system, pointing to several of its features as being particularly refractory to evolutionary explanations. Behe's antievolutionary argument relies on a characteristic he calls "irreducible complexity": the requirement for the presence of multiple components of certain complex systems (such as a multiprotein complex or biochemical cascade) for the system to accomplish its function. As such irreducibly complex systems by definition work only when all components are present; Behe claims they cannot arise by the sequential addition and modification of individual elements from simpler pre-existing systems, thus defying 'darwinian' evolutionary explanations.

By analogy with human 'machines', ID advocates argue that irreducibly complex systems are most likely the product of an intelligent, teleological activity. Several scientists, including ourselves, have criticized Behe's argument, pointing out how irreducibly complex systems can arise through known evolutionary mechanisms, such as exaptation, 'scaffolding' and so on. Nevertheless, with few exceptions^{3–6}, the topic has been explicitly addressed mostly in book reviews^{7–10}, philosophy journals^{11,12} and on the internet, rather than in peer-reviewed scientific publications, which may have allowed it to mostly escape the critical scrutiny of scientists while gaining considerable popularity with the lay public and, in particular, with creationists.

In chapter 6 of *Darwin's Black Box*, Behe claims that the vertebrate adaptive immune system fulfills the definition of irreducible complexity and hence cannot have evolved. Some of his arguments will seem rather naive and misguided to immunologists. For example, Behe argues that working antibodies must exist in both soluble and membrane form, which therefore must have appeared simultaneously because one form would be useless without the other. He also claims that antibodies are completely functionless

without secondary effector mechanisms (such as the complement system), which in turn require antibodies for activation. These putative 'chicken-and-egg' conundrums are easily belied by existing evidence (http://www.talk-design.org/faqs/Evolving_Immunity.html).

Behe also spends considerable time on what he alleges is a hopelessly intractable problem in evolutionary immunology: the origin of the mechanism of somatic recombination of antigen receptor genes. He argues that because variable-diversity-joining recombination is dependent on the coexistence of proteins encoded by recombination-activating genes (RAG proteins), recombination signal sequences and antigen receptor gene segments, it is ultimately too complex to have arisen by naturalistic, undirected evolutionary means because the three components could not have come together in a 'fell swoop' and would have been useless individually. In fact, Behe confidently declares that the complexity of the immune system "dooms all Darwinian explanations to frustration"². About the scientific literature, Behe claims it has "no answers" as to how the adaptive immune system may have originated².

In particular, Behe criticizes a 1994 *Proceedings of the National Academy of Science* paper advancing the hypothesis that the RAG system evolved by lateral transfer of a prokaryotic transposon¹³, an idea initially suggested in a 1979 paper¹⁴ and expanded in 1992 (ref. 15). Behe ridicules the idea as a "jump in the box of Calvin and Hobbes,"² with reference to the comic strip in which a child and his stuffed tiger imaginary friend use a large cardboard box for fantasy trips and amazing physical transformations.

The timing for the criticism could not have been worse, as soon after publication of *Darwin's Black Box*, solid evidence for the transposon hypothesis began accumulating with the demonstration of similarities between the variable-diversity-joining recombination and transposition mechanisms¹⁶ and also between shark RAG1 and certain bacterial integrases¹⁷. Since then, a steady stream of findings has continued to add more substance to the model, as RAG proteins have been shown to be capable of catalyzing transposition reactions, first *in vitro*^{18,19} and then *in vivo*^{20–22}, and to have even closer structural and mechanistic similarities with specific transposases²³. Finally, in 2005, the original key prediction of the transposon hypothesis was fulfilled with the identification of a large invertebrate transposon family bearing both recombination signal sequence-like integration sequences and a RAG1 homolog²⁴. When faced with that evidence during an exchange

on the internet, Behe simply 'shrugged' and said that evidence was not sufficient, asking instead for an infinitely detailed, step-by-step mutation account (including population sizes, relevant selective pressures and so on) for the events leading to the appearance of the adaptive immune system (http://www.pandasthumb.org/archives/2005/06/behes_meaningle.html).

That background set the stage for the crucial face-off at the trial. Kenneth Miller of Brown University, a cell biologist and textbook author who has written extensively on evolution and creationism, was the lead witness for the plaintiffs. Over the course of his testimony, Miller did his best to explain to the nonscientist audience the mechanisms of antibody gene rearrangement and the evidence corroborating the transposon hypothesis. Then, 10 days later, Behe took the stand. During cross-examination by the plaintiffs' lead counsel Eric Rothschild, Behe reiterated his claim about the scientific literature on the evolution of the immune system, testifying that "the scientific literature has no detailed testable answers on how the immune system could have arisen by random mutation and natural selection." Rothschild then presented Behe with a thick file of publications on immune system evolution, dating from 1971 to 2006, plus several books and textbook chapters. Asked for his response, Behe admitted he had not read many of the publications presented (a small fraction of all the literature on evolutionary immunology of the past 35 years), but summarily rejected them as unsatisfactory and dismissed the idea of doing research on the topic as "unfruitful."

This exchange clearly made an impression on Judge Jones, who specifically described it in his opinion:

In fact, on cross-examination, Professor Behe was questioned concerning his 1996 claim that science would never find an evolutionary explanation for the immune system. He was presented with fifty-eight peer-reviewed publications, nine books, and several immunology textbook chapters about the evolution of the immune system; however, he simply insisted that this was still not sufficient evidence of evolution, and that it was not 'good enough.'

We find that such evidence demonstrates that the ID argument is dependent upon setting a scientifically unreasonable burden of proof for the theory of evolution.

Other important scientific points stood out during trial relating to other purported irreducibly complex systems such as the flagellum and the clotting cascade, the nature of science

itself and the lack of experimental tests and supporting peer-reviewed publications for ID. But the stark contrast between the lively and productive field of evolutionary immunology and the stubborn refusal by ID advocates such as Behe to even consider the evidence was undoubtedly crucial in convincing the judge that the ID movement has little to do with science. As Rothschild remarked in his closing argument,

Thankfully, there are scientists who do search for answers to the question of the origin of the immune system. It's the immune system. It's our defense against debilitating and fatal diseases. The scientists who wrote those books and articles toil in obscurity, without book royalties or speaking engagements. Their efforts help us combat and cure serious medical conditions. By contrast, Professor Behe and the entire intelligent design movement are doing nothing to advance scientific or medical knowledge and are telling future generations of scientists, don't bother.

Evolutionary immunologists should be pleasantly surprised by and proud of the effect their scientific accomplishments have had in this landmark judicial case. This commentary is meant to acknowledge their contribution on behalf of the Dover families,

their lawyers and all the activists for rigorous science education who have participated in these proceedings. Most importantly, however, the Dover case shows that no scientific field is too remote from the hotly debated topics of the day and that no community is too small and removed from the great urban and scientific centers to be relevant. Immunologists must engage their communities and society at large in events related to public perceptions about science. Now more than ever, the participation of scientists is essential for the crafting of rational policies on scientific research and science education.

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