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Studying the nuts and bolts of spermatozoa

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When Watson and Crick (1953) first described the 3D structure of the deoxyribonucleic acid (DNA) molecule, they showed the now familiar twisted ladder with a right-hand spiral. Yet now, over 60 years later, DNA is often depicted on book covers and in films with a certain amount of poetic licence: the most annoying of which is when the spiral is twisted to the left. It is clearly an easy mistake to make given the ease by which computer graphics packages are able to flip and rotate images on the screen. Moreover, it can catch out even the most unlikely victims, such as the journal Nature which has unfaithfully reproduced a left-handed DNA molecule on its front cover (Rutherford, 2013). Since this was the very journal where Watson and Crick had first published their iconic paper, you would think that someone in the Editorial Office might have known better. It was clearly a genuine mistake but was incorrect all the same.

Thus, whilst scientists involved in genome biology may wince at the poor depictions of their favourite molecule, those of us who undertake research on spermatozoa quite often do the same about the popular images of our favourite cell. I've lost count of how many times I've argued with artists and animators about, for example, the shape of a sperm head, or the size and shape of the mitochondrial gyre (or lack thereof) in their images used to illustrate books or television programmes I have been involved with. Often it has been more tadpole than sperm. Perhaps more alarmingly are the discussions I've had with students (or other researchers) about such issues which suggest that the collective knowledge of sperm ultrastructure by scientists and clinicians (who should arguably know better) is actually quite

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poor. Thankfully, in this issue of MHR is an outstanding review article by David Mortimer, which pulls together over 70 years of research of sperm ultrastructure using electron microscopy (EM) and other techniques which will hopefully serve as an invaluable reference point for years to come (Mortimer, 2018).

When Antonie van Leeuwenhoek first described human sperm using an early microscope (Leeuwenhoek, 1678), the drawings that were published were surprisingly accurate given the optics available at the time. However, it was the invention of the electron microscope (Knoll and Ruska, 1932) that eventually allowed the inner structure and workings of sperm to be first revealed in hazy detail (Seymour and Benmosche, 1941). Over the following years more structures became clear. For example, it was only in the early 1960's that the protein motor dynein, which has a fundamental role in the movement of almost all flagellated sperm, was discovered (Gibbons, 1963; Gibbons and Rowe, 1965) and subsequently described in the sperm axoneme of sea urchins (Summers and Gibbons, 1971). We now know from the careful EM studies of Burgess et al., (2003) that it is changes in the molecules length when ADP is bound (compared to when it is not) that gives rise to the 'power stroke' and forces the sliding between microtubules and the subsequent beating of the flagellum we observe down the microscope. Clinically, we know the lack of dynein arms is a rare, but important, cause of ciliary and flagellar dyskinesis which can lead to infertility (Afzelius, 1976). Whilst this is arguably the most well-known sperm ultrastructural defect, unfortunately in these days of ICSI, the diagnosis is rarely checked by EM in spite of this almost certainly

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being an inheritable form of male infertility (Ji et al., 2017) and it being relatively easy to do so (Moretti et al., 2016).

In addition to the obvious flagellar defects of sperm, Mortimer (2018) reviews how other defects in the “nuts and bolts” of sperm are related to poor reproductive outcome (sterilizing defects) most of which I suspect are rarely encountered (or poorly diagnosed) within clinics. In part, this is perhaps because ICSI has defocused our minds away from sperm-related problems in recent years, although I also suspect it is also because studies of cell ultrastructure using techniques such as EM became less fashionable for a while. However, Knott and Genoud (2013) recently argued that EM is far from dead but has now re-invented itself into a new force for cell biologists to revisit old problems with new tools. In particular, the developments in cryo-EM (which won the Nobel Prize for Chemistry in 2017 (Cressey and Callaway, 2017), now allows the imaging of molecules and receptors on and within cells as well as giving information about 3D cellular structure with greater clarity (and quicker) than ever before. Perhaps, therefore, it is time for us to engage with these new technologies and apply them to spermatozoa in order to see what more we can learn about this unique and under-studied cell.

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Conflict of interest

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