



Start your Risk-Free Subscription Today ▶

Home : [BioWorld International](#) : [May 18, 2011](#) : Article

Parasite Study Challenges Old Thinking on Inflammation

By Sharon Kingman

BioWorld International Correspondent

LONDON – The discovery of a new type of inflammation is challenging the received wisdom about how white blood cells react when they respond to infection – and could eventually lead to novel therapeutic strategies for treatment of wounds and scars, allergic reactions, autoimmune diseases and cancer.

Until now, the accepted view of how the immune system springs into action when it encounters a pathogen or an injury has been that monocytes in the blood invade the affected tissues and mature into macrophages. Once in the tissues, they respond to signals that direct them to become either M1 cells, which fight and kill microbes, or M2 cells, which can fight parasites such as worms and which are also involved in wound repair.

What a team of researchers from the University of Edinburgh in Scotland has now shown is that, in some circumstances, macrophages already in the tissues can divide rapidly in response to the stimulus, without involving cells that enter the tissue from the bloodstream. In addition, the team, which was funded by the UK Medical Research Council, was able to demonstrate that the cytokine interleukin-4 (IL-4), which directs cells into the M2 pathway, is responsible for driving this response.

Judith Allen, professor of immunobiology at the University of Edinburgh, told *BioWorld International*: "This finding will completely change the way that people think about inflammation. In the past, scientists have believed that inflammation results when white blood cells enter tissue from the blood, and that these macrophages are terminally differentiated – that they can't divide."

Together with an international team of collaborators, Allen has now proved that macrophages already in the tissue can undergo "massive" division without involving cells from the blood. "This process is slower, but much less damaging to the body – it seems to happen when the body can afford to spend a bit of time responding," she added.

The study, reported in the May 12, 2011, edition of *Scienceexpress*, has the title: "Local Macrophage Proliferation, Rather than Recruitment from the Blood, is a Signature of TH2 Inflammation."

Allen's main research interest is the immune response to parasitic infections, particularly those caused by worms. The team knew that M2 macrophages (also known as TH2 macrophages) were important in the immune response to worms. To investigate this further, they were working with an animal model of helminth infection.

"We depleted the monocytes from the rodents' blood, in the expectation that this would prevent recruitment of macrophages to the site of the parasite," Allen said. "But we were thrown when we found that doing this had absolutely no impact on what happened at the site of infection – there were huge numbers of macrophages there."

As a check, they used a classic inflammatory stimulus as a control, in the absence of the parasite. The animals responded as expected, and no macrophages moved into the site of infection. Clearly something different was going on when the parasite was present.

A series of experiments confirmed the macrophages that appeared in the tissues in the experimental animals were derived from a huge expansion of cells found locally in the tissue; they did not come from the blood nor from the bone marrow.

"The difference between what was always thought to happen in classical inflammation – macrophages coming into tissues

from the bloodstream – and what we have described is a bit like the difference between a SWAT team and the local police," Allen explained. "The SWAT team come in very quickly and very aggressively to kill the intruder, but in the process, they cause a lot of collateral damage. But the local police try to keep things calm and under control while they work to sort out the problem."

It may be possible, she added, to harness local macrophage proliferation in situations where rapid repair is required. "If we can figure out the mechanism, then it may be possible to stimulate these macrophages to divide," Allen said. "But there might be other circumstances where you would want to reduce the numbers of these cells; probably many of the macrophages involved in scarring and fibrosis are of the proliferating type."

Likewise, M2 macrophages are good at inhibiting M1 macrophages; the latter are the ones that are good at killing tumour cells and microbes. "So M2 macrophages are bad in the context of tumors. Rather than assuming that these come into the tumor from the blood, they are probably expanding locally," Allen added. "This finding could therefore have an impact on cancer therapy, as well."

Future work will focus on determining the mechanism involved in bringing about the proliferation. The team wants to know the target for IL-4 and the signal that causes the macrophages to divide. Other studies will address whether similar mechanisms are present in humans. "I have little doubt that this type of response is relevant in humans," Allen noted, "because what we have seen is so fundamental."

BioWorld International May 18, 2011

[BioWorld Home](#) | [About BioWorld](#) | [Contact Us](#) | [Copyright Notices](#) | [Terms of Use](#) | [Privacy Statement](#)

Part of Thompson Media Group LLC

[Thompson.com](#) | [Sheshunoff.com](#) | [ASPratt.com](#) | [AHCMedia.com](#) | [BioWorld.com](#) | [CMEweb.com](#) | [ThePerformanceInstitute.org](#) | [ASMIweb.com](#)

Sharon Kingman
Correspondent for BioWorld International
114 Park Road
Chiswick
London W4 3HP
Tel. 020-8742-3451 (from inside the UK)
Tel. +44-20-8742-3451 (from outside the UK)
sharonkingman@clinicalskills.net