When my phone rang and I was told that our article was to be published in *Nature Immunology* (Ribot et al, 2009), I just couldn’t stay put. But even though a few people around me understood my hystericis, I had to explain to many others what this really meant for us: “It’s like an actor receiving an Oscar!”

Our particular Oscar was not for best film, actor or soundtrack, but for a discovery in immunology. Having our work published in this prestigious journal meant that fellow scientists had deemed it noteworthy, and that others would now be able to learn from it and build upon it towards the common goals of understanding how our bodies fight disease and subsequently improving human medicine. Sitting on my shelf, ‘our’ issue may look like just another magazine, but it means as much to me as a trophy in a display cabinet.

The subject of our research is the development of a type of white blood cell, called a T lymphocyte or T cell, in the thymus. T lymphocytes are distinguished from other lymphocytes by a molecule on their surface called a T-cell receptor, which recognises the antigen carried by a specific invader, such as a bacterium or virus.

T cells are generally considered part of the adaptive immune response, because they not only eliminate an invader (and the cells it has invaded), but also produce memory cells. As their name implies, these memory cells ‘remember’ that invader for as long as the animal lives, so this immune response adapts very quickly: if that same invader strikes again, the memory cells will recognise and destroy it. This adaptive immune response, which only vertebrates possess, is activated by the innate
immune response, the non-specific defence system found in all classes of animal and plant life. The innate immune response is the first line of defence: the initial reaction to (and attempted elimination of) invaders. Unlike the adaptive immune response, the innate immune response does not confer long-lasting or protective immunity, but it is a swifter and more general response.

Our work focuses on a specific type of T cell, the gamma delta (γδ) T cell, which is seen as an evolutionary bridge between the adaptive and the innate immune responses. γδ T cells form subtypes with different functions, depending on what tissue they are found in and which specific T-cell receptor they bear. Even though there is a growing consensus about the importance of γδ T cells, little is known about their behaviour or development, and scientists haven’t yet found any molecular markers that they can use to identify the different subtypes.

In our research, we looked at a protein that we suspected might be a potential marker for one subtype of γδ T cells. This protein, called CD27, is a membrane receptor involved in cellular communication.

We found that our suspicions were well founded: CD27 can be used to identify a particular subtype of γδ T cell. But what was most interesting...
was that we discovered that the presence of this protein doesn’t merely characterise this subtype of γδ T cell, it actually drives its formation. Within the thymus, the precursors of γδ T cells that mature in the presence of CD27 (CD27+) produce a cytokine called interferon-gamma (IFNγ) whereas cells that mature without CD27 (CD27-) produce primarily a different cytokine, interleukin-17 (IL-17). The presence or absence of the cytokine CD27 thus defines which subtype a γδ T cell will belong to (see diagram above). The two cytokines IFNγ and IL-17 play an important role in the immune response, with very distinct consequences: those T cells producing IFNγ will play a crucial role in fighting viruses and tumours, whereas those producing IL-17 are associated with autoimmune diseases such as multiple sclerosis.

γδ T cells play an important role in initiating a quick immune response to various parasites, including the malaria parasite *Plasmodium*. In humans, this parasite multiplies in the liver, and then spreads to the blood stream, infecting red blood
Ana de Barros was born in Lisbon in 1983, and at the age of 19 moved to Newcastle, UK, where she graduated in genetics. She then stayed in the UK to do an MSc in biomolecular archaeology in Manchester. After working for 3 months in a lab in Athens, Greece, doing stem cell research, Ana went back to Portugal in 2007, where she started her PhD in immunology at the Instituto de Medicina Molecular in Lisbon\(^1\). She is interested in scientific journalism, as it brings together communication and science. Outside the lab, she is involved in the arts and has a band where she plays the guitar, writes songs and sings. Ana also does a lot of photography and enjoys travelling.

Confocal image of human $\gamma\delta$ T cells (in red) attacking tumour cells (in yellow)

Image courtesy of Bruno Silva-Santos’ lab

In short, we were the first to describe a function for CD27 in T-cell precursors in the thymus – and the fact that Nature Immunology decided to publish our article is recognition of just how important these findings are. As our group leader, Bruno Silva-Santos, explains, “We are now investigating the analogous processes in human cells. Our long-term goal is to be able to manipulate $\gamma\delta$ T cells for therapeutic purposes such as fighting autoimmune diseases and cancer.” We still have a lot of work ahead of us, but this recognition of what we have already achieved reminds us that it is all worth it.

Long after I had hung up the phone, then finished explaining my excitement, I still couldn’t stop smiling.

References
Ribot JC, deBarros A, Pang DJ, Neves JF, Peperzak V, Roberts SJ, Girardi M, Borst J, Hayday AC, Pennington DJ & Silva-Santos B (2009) CD27 is a thymic determinant of the balance between interferon-$\gamma$ and interleukin 17-producing $\gamma\delta$ T cell sub-sets. Nature Immunology 10: 427-436. doi:10.1038/ni.1717

Web references
w1 – Find out more about the Instituto de Medicina Molecular in Lisbon here: www.imm.fm.ul.pt

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