The ‘intelligent’ human immune system can respond naturally to fight cancer

Dr Xuemei Zhong, PhD, is Assistant Professor of Medicine at the Boston University School of Medicine. Her research looks at how the ‘intelligent’ human immune system can be stimulated to fight diseases. The ‘intelligent’ human immune system can naturally respond to fight cancer without reliance on high doses of drugs and short-lived therapies, with a particular focus on a process called immunosurveillance.

The part of the immune system that recognises and removes cancer cells naturally is called the ‘immunosurveillance’ system. This term describes the body’s ability to recognise and remove harmful cells. It differs from the conventional immune response in that it does not cause significant or systemic inflammation in order to remove threats to the body. Instead, it is an ongoing, self-renewal maintenance process that operates in the background.

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SURRENDERING THE VETERAN

Cancer treatments that stimulate the immune system typically induce the conventional inflammatory response. However, the effects of such methods are usually short-lived and difficult to control because cancer cells adapt rapidly and develop drug resistance.

Most cancer therapies focus on manipulating a single factor, such as a signal pathway or biomarker, without considering the ‘ying and yang’ sides of the same factor. For example, if you remove a causative factor, you may have removed the ‘attraction factors’ for healing. Dr Zhong says this slows down healing and explains the short-lived and ineffective nature of many current treatments.

LEARNING FROM FAILURE

When the body’s natural immunosurveillance system fails to remove cancer cells quickly enough, they accumulate and cause disease. By understanding what happens when this process goes wrong, Dr Zhong and her team aim to find methods of improving the system, and therefore of preventing cancer.

Harmful foreign bodies stimulate an immune response, and this allows the system to learn, meaning that the likelihood of infection is reduced the next time the body is exposed to the same factors. However, the failure of cancer prevention is a little different. According to Dr Zhong’s hypothesis, one of the causes of modern day failure of cancer prevention is ‘deviation and exhaustion’ of the immunosurveillance system with multiple on-going battles. This hypothesis is supported by the mounting evidence reported that the risk of cancer is increased in obesity patients and other chronic lifestyle diseases.

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In order to find ways of ‘restoring’ or ‘rebooting’ immunosurveillance, Dr Zhong has been focusing on specific and unique cells that are critical in the immunosurveillance system.

BUILDING AN ARTILLERY

Conventional B lymphocytes as we know from our biology text books are the B cells which produce antibodies against foreign bodies and inhibit their activity. Conventional B cells are also termed B-2 B cells to differentiate from the B cells that Dr Zhong’s group has been studying in mice, which are termed B-1 B cells.

Both B-1 and B-2 B cells can fight against foreign invaders. However, B-1 B cells are also designed for immunosurveillance with their unique natural IgM antibodies and
It is difficult to manipulate the immune system without affecting its own healing mechanism. The ultimate goal for cancer immunotherapy is to restore immunity and then let it work on itself.

How crucial has your other work on diseases like lupus been in informing your research on cancer therapies?

Great question. We started to study the same type of B cells in autoimmune diseases like lupus. That was based on a traditional concept that autoimmune diseases are caused by auto-antibodies that recognise self-antigens and consequently bring self-destruction to our body. Since the B cells we were interested in recognise mostly self-antigens, we thought they could be the cause of autoimmune diseases. Despite our finding that these B cells do generate antibodies that recognise self-antigens, our data showed something unique and contrary to what we hypothesised.

The auto-antibodies from these B cells do not just react to a single epitope of an antigen as with traditional B cells. Instead, the same antibody reacts to various self-antigens simultaneously. All these antibodies are IgM isotype with low affinity but high avidity and their DNA sequence is germ-line coded; they were the ‘original design’, not the result of external stimulation such as vaccination or infection. They exist in animals that have been born totally pathogen-free, sterile environments. As reported by other groups, these IgM auto-antibodies are very different from those pathogenic auto-antibodies in autoimmune patients. Thus, this led us to hypothesise the function of these B cells in the opposite direction – their protective functions rather than pathogenic functions. This revelation led to our current research on the role of the IgM in the immunity of cancer because cancer cells are mostly ‘self’ and need to be recognised and removed. We believe the antibodies produced by NIMPAB cells recognise certain pattern of cancerous cells rather than a single marker. Moreover, cancer cell elimination happens every day in healthy individuals without eliciting any autoimmune response. Our study led us to believe NIMPAB cells are the best candidate for such a job.

Are NIMPAB cells the only type of cells that play a central role in coordination?

No – in our immune system, no single type of cells or status of cells can work alone. It is always teamwork. However, NIMPAB cells play a very unique role. To put it in a metaphorical way, in healthy status, NIMPAB cells are like a custodian who patrols our body to remove senescent cells, cancerous cells, metabolic trash and toxins etc. In chronic disease status, NIMPAB cells are like rising liaisons or even commanders on the battlefield. They identify the problem as they are equipped with unique tools that others don’t have, i.e., natural IgM antibodies and surface IgM and other receptors. They act as primary wave of solutions, secrete antibodies, regulatory cytokines to adjust inflammation level and phagocytose target cells and cell debris or viruses. They relay the information to other cells by antigen presentation and cell-cell contact or by secreting chemokines to remotely recruit proper team members or soldiers to the battle ground. In summary, NIMPAB cells not only are the best type of cells but play a central role in coordination.

Would an enhanced immunosurveillance response be more effective as a preventative or as a curative treatment for cancer?

The answer is ‘both’. From a preventative point of view, the amount of NIMPAB cells and natural IgM in our body may indicate subclinical health status. Naturally boosting them may tip the scales and prevent the accumulation of small problems from mounting into chronic disease. In terms of treatment, supplementing NIMPAB cells and natural IgM will change the outcome of the on-going battle; like when your commander or troops are exhausted in a long battle and you suddenly airdrops fresh troops and a new commander to the front line.

How well do your findings translate from the mouse model to humans?

We have identified NIMPAB cells in both the mouse model and humans. We are confident that given the essential finances, personnel, and time, we will absolutely translate these into clinical treatment.

Can these treatments be applied to other diseases?

Absolutely. As we mentioned before, NIMPAB cells are the custodians of our body. Cancerous cells are one of the many things they take care of. All modern-day chronic diseases are a result of an imbalanced internal environment and the resultant accumulation of certain forms of cells, molecules and toxins in our body. NIMPAB cells and their natural IgM can benefit all kinds of chronic issues. One clinical example is IGV. Through currently unknown mechanisms, IGV can treat many diseases beyond its original use as a mere IgG supplement to help immunodeficiency patients battle infection. As large-scale industrial production techniques advance, you will see massive production of natural IgM for the treatment of many diseases.