

Scientists make headway for cancer treatment and cancer prevention with landmark discovery

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Scientists at A*STAR's Institute of Molecular and Cell Biology (IMCB) have made a landmark discovery in the battle against the rapid spread of aggressive cancers associated with PRL-3 oncoprotein . Contrary to the current accepted theory that antibodies can only bind to cancer proteins found on the cancer cell surface, the IMCB team led by Dr Zeng Qi is the first to discover that antibodies can in fact directly target intracellular oncoproteins like PRL-3 that reside within the cancer cells to suppress cancer growth successfully. This breakthrough finding will pave the way for more targeted solutions for cancer treatment and also offers hope for cancer prevention.

The leading cause of death by [cancer](#) is [cancer metastasis](#) – the rapid and often fatal spread of cancer cells from the primary tumour to other parts of the body. PRL-3, which stands for "Phosphatase of Regenerating Liver 3", is a key protein linked to cancer metastasis. PRL-3 is commonly overproduced in many types of aggressive lung, liver, kidney, bone and breast cancer. For example, colorectal cancer and breast cancer, the top five most deadly cancers in the world and also the number one most common cancers in both male and female population respectively in Singapore , are frequently associated with elevated levels of PRL-3 phosphatase. PRL-3 is therefore an ideal target for cancer diagnostics and treatment.

Traditionally, oncoproteins like PRL-3 phosphatase which reside within

the cancer cells were thought to be inaccessible by [antibodies](#) because it is widely accepted that antibodies are too big to cross the cell membrane. This study suggests that cancers could be effectively treated through the direct introduction of antibodies to target the PRL-3 oncoprotein inside the cancer cell. Likewise, vaccination with PRL-3 antigen to prevent cancer can be administered to induce the body's immune system to produce PRL-3 antibodies that will directly target the PRL-3 oncoprotein within the cancer cell.

Said Dr Zeng, who first identified PRL-3 phosphatase in 1998, "We are very excited because this study showed for the first time that it is possible to successfully suppress [cancer growth](#) by direct targeting of intracellular oncoproteins, such as PRL-3, with the respective cancer-specific antibodies." Using mouse models in this study, by directly introducing PRL-3 antibodies into the mice, the scientists observed a 70% to 90% reduction of tumours caused by PRL-3 expressing cancer cells. This significant reduction is also achieved by vaccinating the mice with PRL-3 antigen to produce antibodies that could specifically target PRL-3-expressing cancer cells.

To prove that antibodies can indeed directly target other intracellular oncoproteins as a general phenomenon, the team also performed the experiment with two different representative intracellular proteins, EGFP and mT oncoprotein. It was observed that the antibodies introduced to the mice could directly target the intracellular oncoproteins to dramatically retard tumour progression.

Added Dr Zeng, "This means that a whole new list of intracellular oncoproteins previously thought to be untargetable by therapeutic antibodies or vaccinations can now be potentially targeted. This will expand the scope for tailor-made antibody therapy as well as usher in a new era of tailor-made cancer vaccines."

Professor Sir David Lane, Chief Scientist of A*STAR said, "Dr Zeng's breakthrough discovery is a fine example of how years of basic research lay the foundation for advancement in translational medicine. This study has introduced a potential paradigm shift in the ways we target [cancer cells](#) with antibodies and vaccines. It has opened unexpected doors of possibilities in cancer and immunology research. Much further work will of course be needed to establish the safety and efficacy of this approach in cancer patients but it indeed paves the way for more targeted [cancer treatment](#) & offers new hope for [cancer prevention](#)."

Said Dr Zeng, "Cancer affects people regardless of age, gender, wealth or social status. It represents a tremendous burden on patients, their families and the society. Existing antibody therapy for cancer treatment is very costly. I hope that our research will pave the way for cancer vaccination to become a mainstream cancer treatment that is both effective and affordable for the cancer patients. Especially for individuals who are genetically pre-disposed to specific types of cancer, tailor-made vaccination may one day be able to prevent cancer before it strikes."

More information: The research findings described in this news release can be found in the 7 Sept 2011 issue of *Science Translational Medicine* under the title, "Targeting Intracellular Oncoproteins with Antibody Therapy or Vaccination" by Ke Guo, Jie Li, Jing Ping Tang, Cheng Peow Bobby Tan, cheng William hong, Abdul Qader O. Al-Aidaroos, Leyon Varghese, Caixia Huang, and Qi Zeng.

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