Small and mighty medical gains

From a pharmaceutical foundation to nanomedical breakthroughs.

Dr Susan Hua's research is proving that some of the greatest gifts to human health can come in the tiniest of packages. With a research focus in the cutting-edge field of therapeutic targeting, Dr Hua is making new and existing medicines work better with fewer side effects and less toxicity through nanomedicine.

Nanomedicine is the application of nanotechnology to medicine, and is a revolutionary field made possible by the convergence of chemistry, biology, mathematics, physics and engineering. This rapidly advancing area has the potential to transform the way we implement healthcare.

As a clinical pharmacist, Dr Hua is well aware of the side-effects caused when drugs harm healthy cells in the body. With cancer treatment, the side-effects of chemotherapy can rapidly decrease the quality of life of patients by causing debilitating side effects such as fatigue, nausea, vomiting, pain, hair loss, decreased blood cell counts and organ damage.

Quality of life affected

For people living with chronic pain, the treatments can sometimes feel worse than the cure. "Chronic pain affects the quality of life of so many people, with current treatments limited by sedation, confusion, gastrointestinal upsets, respiratory depression and organ damage," Dr Hua explains. After several years working as a pharmacist, Dr Hua moved into research to explore ways to improve existing treatment options for people who need medications to manage their conditions. "Most conventional medicines are essentially high-doses of free drugs that are distributed to all parts of the body," Dr Hua explains. "This means they're not very efficient and have an increased risk of adverse effects."

To reduce side-effects and increase the effectiveness of medications, Dr Hua has created nano-vehicles, tiny products which can work like a GPS to drive medications directly to the affected site in the body. The therapeutic agents are locked into the nano-vehicles which are then delivered directly to the site of disease. Once at the target site, the vehicles will open and deliver the medication precisely where it is needed.

Translational Nanopharmaceutics Laboratory and Research Program

Since joining the University of Newcastle in mid-2010, Dr Hua has established this program to focus on therapeutic targeting utilising novel drug delivery platforms in biomedical applications. The goal of her research is to use nanotechnology as a platform to study novel mechanistic pathways, as well as to develop more efficient therapeutic systems.

Dr Hua's research expertise covers the areas of advanced pharmaceutical formulation, in vitro cellular studies, and preclinical *in vivo* animal studies. This expertise provides a solid foundation to formulate and evaluate new drug delivery systems and to apply them to pathological disease states, in order to assess potential clinical applicability and identify novel therapeutic targets. Dr Hua's research provides a platform for the translational development of targeted therapeutics that will ultimately provide a novel therapeutic strategy in clinical disease management.

Nanomedicine has the potential to improve the way we treat a range of health conditions such as acute and chronic pain, reproductivepathologies, gastrointestinal diseases, skin conditions,

infections, and cancer. By loading bioactive compounds and imaging agents into carriers that are designed to bypass biological barriers which would ordinarily degrade or hinder their accumulation at the target site, Dr Hua is developing safer and more effective medications and diagnostic agents. This allows for maximum targeting efficacy as lower and less-frequent doses are required. Thus, it also reduces side effects and toxicity.

In a world-first study recently published in the American Journal of Obstetrics and Gynecology, Dr Hua collaborated with pregnancy researchers Laureate Professor Roger Smith and Dr Jonathan Paul to successfully use nanomedicine to target a hormone sensor predominantly found in the uterine muscle. "This project is exciting as we are able to deliver drugs specifically to the uterus using nano-vehicles targeted to the oxytocin receptor," Dr Hua explains. "Oxytocin receptors are highly expressed in the uterus during the labour process, which makes it an ideal target for targeted drug delivery."

Nanomedicine changes the game

The technology may allow a new generation of labour drugs to be developed. It can also be used to improve the delivery of existing therapies that deter or induce uterine contractions, which will allow lower dosages to be administered and fewer off-target effects. "This means we are able to develop more effective medicines to treat pregnancy-related complications that are also much safer for both the expectant mothers and unborn baby," Dr Hua explains.

The team spent four years optimising and evaluating the system in both laboratory modelling and human uterine muscle tissue. The next stage is to conduct further safety studies in primate models before clinical trials to help characterise the biodistribution of the novel drug delivery system to confirm reduced maternal and foetal side effects.

Dr Hua is also using her nanopharmaceutics expertise to collaborate with clinical gastroenterology researchers, Laureate Professor Nick Talley and Professor Marjorie Walker, to develop new treatments for gastrointestinal diseases by targeting inflammatory cells in the gut. Gastrointestinal diseases are a major cause of illness in Australia, with many conditions limited by existing treatment options. "We have developed innovative platforms that allow imaging and therapeutic agents to bypass the mucosal defence mechanisms in the gut to better diagnose and treat chronic inflammation", Dr Hua explains.

A number of her other projects are focused on translational pain research in the areas of peripheral analgesia and inflammation. Using preclinical models of acute and chronic pain, her team is interested in using nanotechnology as a means to investigate peripheral pathways that drive disease and to develop novel treatment platforms. "Our group and others have demonstrated that opioids display potent peripheral analgesic effects in various types of pain, including arthritis, acute tissue injury, bone pain, and post-surgery," Dr Hua explains.

"The effect of peripheral opioids on inflammation has only recently been studied, and our results have potentially revealed a variety of complex regulatory activities in various tissues of the body," Dr Hua concludes. This study can help determine the place for systemically and locally administered opioids in pain management, which would provide new therapeutic strategies for the treatment of chronic pain.

Dr Hua was awarded the *2015 HMRI Early Career Researcher of the Year Award, 2016 NSW Young Tall Poppy Science Award*, and *2016 Newcastle Innovation® Excellence in Innovation Award,* for her significant and valued contribution to the research community.

Dr Susan Hua, Pharmacist and Nanomedicine researcher at the University of Newcastle