Cancer gene therapy from camels

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Nanobodies produced from camel blood have unique properties, which can be used in future drug development. New research published in *Journal of Controlled Release* confirms that camel blood can help scientists in the fight against cancer.

Members of the camelid family have particular heavy-chain antibodies. These antibodies can be used to clone nanobodies, which are antibody-derived therapeutic proteins. One of the most powerful advantages of nanobodies is that they can be easily attached to other proteins and nanoparticles by simple chemical procedures.

Scientists at the Department of Pharmaceutics and Analytical Chemistry, University of Copenhagen, have designed nanoparticle systems of smaller than 150nm that are decorated with nanobodies expressing high specificity for the cancer marker Mucin-1, which is connected to breast and colon cancer.

Research supports aim for safer nanomedicines

"This is a very effective and a highly promising approach in experimental cancer gene therapy, while minimising adverse-related reactions to cancer nanomedicines. Futhermore the research supports our aim for rational design and engineering of effective and safer nanomedicines for the future. We have taken the first step, but of course more work is needed to support the efficacy of this system for cancer treatment," says Professor Moein Moghimi.

Professor Moghimi works at the Department of Pharmaceutics and Analytical Chemistry at the Faculty of Pharmaceutical Sciences where he heads the Centre for Pharmaceutical Nanotechnology and Nanotoxicology, which is supported by the Danish Ministry of Science, Technology and Innovation.

The procedures for camel immunisation, generation and purification of the Mucin-1 nanobody were done by Dr. Fatemeh Rahbarizadeh's team at the Medical Biotechnology Department of the Tarbiat Modares University in Tehran. Dr. Rahbarizadeh is currently visiting scientist at the University of Copenhagen.

Two postdocs, Davoud Ahmadvand and Ladan Parhamifar, from the Faculty of Pharmaceutical Sciences, University of Copenhagen, were also involved in the lab work.

Size and properties matter

Compared to other protein-based drugs, nanobodies are very small. They are ten times smaller than intact antibodies. They are also less sensitive to temperature and pH changes and can be easily linked to nanoparticles and other proteins. These properties make nanobodies very interesting for targeting of cancer cells.

The recently published article in Journal of Controlled Relase describes how a Mucin-1 nanobody was linked to specialised nanoparticles made from polymers carrying a killer gene known at truncated-Bid. When expressed, the gene product triggers cells to commit suicide.

However, the expression of the killer gene was under the control of the cancer-specific Mucin-1 promoter as to avoid non-specific cell killing. These procedures are also referred to as "transcriptional targeting", which can prevent normal tissue toxicities associated with other cancer

treatments. Indeed, the formulation proved to be highly effective in killing cancer cells expressing the Mucin-1 marker, while no harm was done to the normal cells or cancer cells that did not express the Mucin-1 marker.

The efficacy of these nanoparticles is now being tested in animal models.

Another exciting development is that the team has now purified a second and a highly effective nanobody against another cancer marker (Her-2) expressed by certain breast tumors.

Provided by University of Copenhagen