Where is monoclonal antibody therapy leading us?

While there is something of a lag in new therapies for veterinary use, we are gradually seeing more monoclonal antibody products becoming available on the veterinary market, with the recent release of two anti-nerve growth factor therapies bedinvetmab (Librela) and frunevetmab (Solensia) for the management of osteoarthritis in dogs and cats respectively. As this area expands, monoclonal solutions for the management of acute diseases are also being released, for example in COVID-19 treatment, expanding the possibility of more specific treatments for serious viral disease; a real step forward from current therapies that tend to be targeted broadly against viral DNA/RNA replication with significant potential for side effects.

For many of us, this group of agents did not feature as part of our undergraduate pharmacology, so what are they, are they safe and how effective might they be? Well, the origin of this technology was to identify antigen-specific plasma cells that produce antibodies to that specific antigen, and then to fuse these cells to myeloma cells to make them immortal. The process is relatively inefficient, but specialist medias have been developed to promote hybridoma growth. The rapid evolution of molecular techniques has led to a variety of other solutions to monoclonal antibody production, such as phage display or single B cell culture, also allowing their applicability to multiple species.

The main issue that faced early therapies was the host immune response, as the monoclonal antibody produced was related to the species in which it was created (usually rabbits or mice). This led to the development of processes to humanise the resulting monoclonal and minimise the likelihood of it being recognised as foreign. Over time, the use of transgenic mice, phage display and single B-cell cloning have resulted in fully human monoclonal antibodies. It is also now possible using CRISPR/Cas9 and other technologies to produce recombinant monoclonal anitbodies from viruses and yeasts that allow multiple monoclonal anitbodies with slightly different amino acid sequences, which can then be screened for stability and ability to recognise the antigen. However, the final product is not completely homogeneous as changes in the antibody structure will occur during the manufacturing process as a result of various reactions such as deamination or glycosylation.

The key things to remember about these products are that they are species-specific (use in another species risks both a lack of efficacy as the monoclonal antibody may not recognise the target or produce a significant immune response as the antibody is foreign) and they are target-specific to the receptor, so they may have very limited action outside of the specific indication for which they were created. By being more target-specific, effects should be more predictable and side effects less, but this is also a potential weakness as if the pathway being targeted is not responsible for the clinical presentation, the drug will not have a suitable action.

Inherently, this means that our diagnoses need to become more specific to effectively deploy these products. Nonetheless, this is a really exciting opportunity for veterinary medicine and with many other monoclonal antibody therapies in development, there is hope that we may have some new drugs in our armoury to treat previously intractable diseases for which current therapies have significant side effects. CA

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