# Laboratory discovers new antibody function

January 29 2016, by Ann Blackford

The laboratory of Dr. Jayakrishna Ambati of the University of Kentucky College of Medicine and an international team of researchers from Italy, United Kingdom, Japan, France, The Netherlands, Australia, Sweden and Czech Republic, detail the discovery of a previously unrecognized function for antibodies in two articles this week in the inaugural issue of *Signal Transduction and Targeted Therapy*, a journal of the Nature Publishing Group.

The immune system produces antibodies to recognize and bind to specific features found on pathogens such as bacteria and viruses. This results in destruction of the pathogen by white blood cells that recognize the antibody. Antibodies are generally thought to only protect the body from infectious disease.

However, the international consortium led by Ambati found that the most abundant class of antibodies, known as IgG1s, also generically block blood vessel growth, an unexpected finding with far-reaching implications. Therapeutic human antibodies, most of which are IgG1s and account for more $75 billion in annual sales worldwide, are commonly used to treat various diseases such as arthritis, psoriasis, inflammatory bowel disease, leukemia and asthma.

Ambati's laboratory found that FDA-approved and widely used monoclonal antibodies such as Humira, Campath, Lemtrada, Arzerra, Xolair, Synagis, Actemra, and Avastin could inhibit blood vessel growth independent of their intended targets. Moreover, the researchers also showed that intravenous immunoglobulin (IVIG), a low-cost mixture of

human antibodies used to treat many autoimmune diseases, also blocked blood vessel growth.

These two groundbreaking studies used not only preclinical models of macular degeneration, peripheral arterial disease, colon cancer, but also verified the clinical relevance of their findings by examining biopsied tissue from organ transplant patients before and after IVIg therapy.

"Given the widespread use of monoclonal antibodies for many diseases, both in the eye and beyond, these findings have broad clinical implications," said Ambati, the Dr. E. Vernon & Eloise C. Smith Endowed Chair in Macular Degeneration.

Ambati hopes these findings mean patients may one day have a cheaper alternative to current high-priced antibody therapeutics. In addition, these studies suggest the need for caution in prescribing IVIG or monoclonal antibodies for patients with preexisting blood vessel disease.

**More information:** Sasha Bogdanovich et al. Human IgG1 antibodies suppress angiogenesis in a target-independent manner, *Signal Transduction and Targeted Therapy* (2016). DOI: 10.1038/sigtrans.2015.1

Reo Yasuma et al. Intravenous immune globulin suppresses angiogenesis in mice and humans, *Signal Transduction and Targeted Therapy* (2016). DOI: 10.1038/sigtrans.2015.2

Provided by University of Kentucky