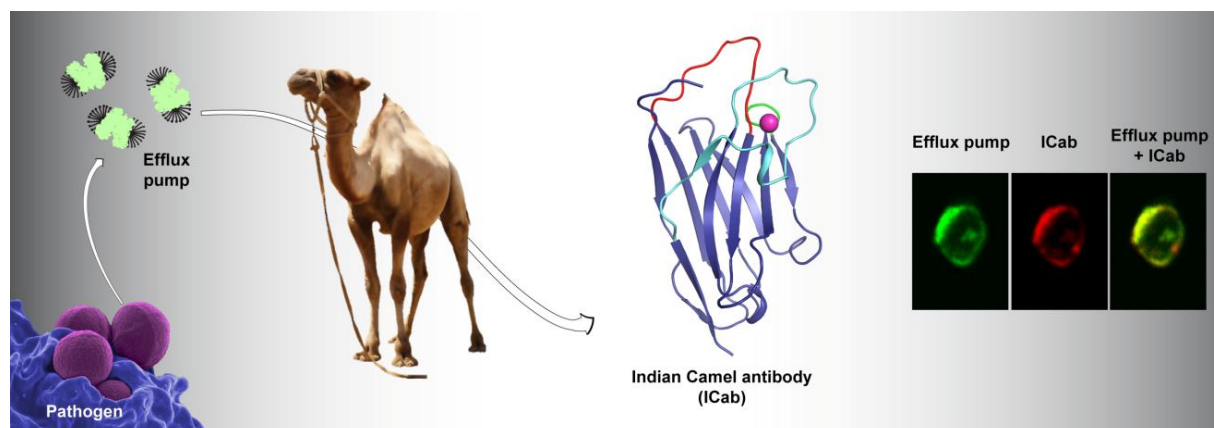


## Success Story: Efflux pump detection with a camel antibody

Antibodies are powerful tools widely used for both diagnostic and therapeutic applications against numerous diseases. Conventional antibodies, for instance from humans, are large “Y-shaped” molecules that comprise heavy and light chains. Despite their widespread biomedical applications, conventional monoclonal antibodies are cumbersome and expensive to prepare using hybridoma technology. Interestingly, camels, llamas and sharks possess specialized antibodies (VHH) made up of only the heavy chain. The ability to target an antigen resides in a single protein domain that is one-tenth the size of a monoclonal antibody. Despite the compact size of conventional antibodies, these rugby ball-shaped antibodies bind their targets with very high affinity. Camel antibodies also have structural features that can access cavities, pockets and tunnels on the surface of their protein targets.

VHs from an Indian Camel (ICab) was isolated from camel immunized against a drug transporter that is implicated in the efflux of antibiotics from a superbug, methicillin-resistant *Staphylococcus aureus*. A screening technology referred as yeast surface display method was employed to identify the ICabs that can easily be harvested in large quantities from bacteria, thus, making the production very cost-effective. We solved its structure using X-ray crystallography and found a zinc ion bound to the region of ICab that is essential for antigen-antibody interactions. This novel modification, that increases the stability of the ICab, was previously never observed in any other camel or llama antibodies known so far. This ICab binds with the transporter on its extracellular side, thereby allowing its use as a potential detection tool or as an inhibitor of superbug efflux pumps. More importantly, these ICabs can be employed as widespread substitutes for conventional antibodies in numerous biotech and biomedical applications.



Source: Modified from <https://www.iisc.ac.in/efflux-pump-detection-with-a-camel-antibody/>

DBT Sponsored Research Project: **Isolation of camelid antibodies as antibiotic adjuvants against multi-drug efflux transporters of methicillin resistant *Staphylococcus aureus*** ( PIs: Aravind Penmatsa, IISc & Dr. Rakesh Ranjan, NRCC-Bikaner)

### Publications:

1. Kumar, S., Mahendran, I., Athreya, A., Ranjan, R. & Penmatsa, A. **2020**. Isolation and structural characterization of a Zn<sup>2+</sup>-bound single-domain antibody against NorC, a multi-drug efflux transporter in bacteria. **J. Biol. Chem.** 295(1): 55-68.
2. Sushant Kumar, Arunabh Athreya, Aushutosh Gulati, Rahul Mony Nair, Ithayaraja Mahendran, Rakesh Ranjan and Arvind Penmatsa. **2021**. Structural basis of inhibition of a transporter from *Staphylococcus aureus*, NorC, through a single-domain camelid antibody. **Communications Biology** DOI 10.1038/s42003-021-02357-x
3. Puja Majumder, Shahbaz Ahmed, Pragya Ahuja, Arunabh Athreya, Rakesh Ranjan and Aravind Penmatsa. **2023**. CryoEM structure of QacA, an antibacterial efflux transporter from *Staphylococcus aureus*. **The EMBO Journal** DOI: 10.15252/embj.2023113418