

Interview with Srinivasa Rao, PhD., Senior Scientist at Phenomenex

An accomplished scientist in monoclonal antibody and protein analytical development, purification, and characterization, and has also designed columns, applications, and method developments, Srinivasa Rao, PhD. is a man of biochemistries.

However, like many who go into the field of biochemistry, Dr. Rao started off with the dream of becoming a medical doctor, the first in his family in fact! His father was the only one in their hometown to finish his law degree, then two of Dr. Rao's brothers followed in their father's footsteps to become lawyers. Dr. Rao wanted to stand out from the crowd.

But that dream was cut short. Acceptance into medical school in India by merit is exceptionally limited, due to caste and class-based reservation system. And even though Dr. Rao never became the medical doctor he once thought he would be, his son went on to fulfill the dream.

Dr. Srinivasa Rao didn't let this deter him. He worked harder than ever and was accepted into the 2nd best option to going into medical—biochemistry for his master's program and later for his Ph.D.

He worked with some of the biggest names in the field, and at some of the most prestigious laboratories in the world, such as the Albert Einstein College of Medicine, New York University, and Ranbaxy Laboratories. During his career he has managed Ph.D. level scientists and led the development of a portfolio of industry-leading bio separation tools and applications for mAbs, proteins, peptides, DNA and carbohydrates.

He has extensive experience in cancer drug target evaluation and drug screening and was

one of the first to characterize the taxol binding site on microtubules using photo-labeling approach. Dr. Rao also has extensive scientific writing experience with several publications in peer-reviewed journals.

Along with his spectacular strides in science, Dr. Rao is also a strong advocate for giving back to his community. He has been volunteering with the Sankara Eye Foundation and the Silicon Andhra organization for more than 16 years.

India has the largest blind population in the world, mostly due to lack of resources to help heal cataracts. The goal of the Sankara Eye Foundation (SEF) is to eradicate the cases of curable blindness by opening hospitals in every state of the country. Dr. Rao has been working as a volunteer since 2001, manning booths and helping to spread the organization's vision and to raise funds. So far SEF has completed more than 1.5 million cataract surgeries and built 9 hospitals in India.

The other non-profit organization that Dr. Rao is passionate about is Silicon Andhra, a group whose goal is to maintain and perpetuate the Telugu Samskruti (Culture), Sahityam (Literature) and Sampradayam (Tradition) among the Telugu speaking people of USA. Silicon Andhra is committed to raise the awareness of the Telugu culture among the denizens of US and integrate it seamlessly with the mainstream US culture by organizing unique cultural and literary events that depict the rich cultural heritage traditions and arts of Andhra Pradesh. Silicon Andhra represents the aspirations of more than 30,000 strong Telugu speaking people in the Silicon Valley, California.

After hearing the story of how Srinivasa Rao came to be known as the great and powerful ion exchanging guru, we wanted to pick his brain. See below for answers to a few of the most asked questions we receive from those in the biotherapeutics industry.

1. Why do researchers perform charge variant analysis?

Monoclonal antibodies (mAbs) are developed by pharmaceutical and biotechnology companies for various therapeutic applications. During synthesis, formulation and storage, they are susceptible to several types of modifications. These impurities/changes can lead to toxic implications when administered to patients. Therefore, complete characterization of mAbs is required by the FDA and other regulated authorities.

mAbs express intrinsic micro-heterogeneity. In addition, chemical modifications of mAbs, such as sialylation and deamidation, introduce additional negative charges to the molecules, leading to acidic variant species. C-terminal processing of lysine residues introduces one or more additional positive charges to the molecules and generates basic variant species. Such acidic and basic variants due to their charge differences can be separated from the main isoform using ion exchange chromatography-based separations.

Among the analytical techniques, IEX is best suited for characterizing charge variants of intact and fragmented mAbs. Among different IEX modes, cation-exchange chromatography (CEX) is the most suitable approach for mAb analysis and purification due to majority of their isoelectric points (pI values) are between 6 and 9.

2. What techniques are typically used to determine charge heterogeneity?

Differences in charge is typically determined by Ion exchange chromatography, Isoelectric focusing and Imaging Capillary Isoelectric focusing techniques. Since most mAbs typically have higher isoelectric points (pIs between 6 to 9), cation exchange chromatography is preferred technique among IEX techniques.

3. You are the mastermind behind the new bioZen 6 µm WCX column. Can

you tell us why you're excited about this new development?

It is really our team effort. We are excited about it because we created this cation exchange phase with unisized particles and with proprietary chemistry. Unisized particles helped us to control the optimal reproducible grafting process as well as lowered column back pressure. Also, we make sure that it works for a variety of customer applications where pH gradients and salt gradients-based separations are routinely used. In addition, we carefully examined the strengths and weaknesses of the competition, and successfully overcome the drawbacks to provide the best cation exchange chromatography solution for our customers.

Don't forget to explore the latest project by Dr. Srinivasa Rao, the bioZen™ WCX Ion-Exchange Column! Guaranteed to separate proteins from acidic and basic protein variants, and you can expect excellent recovery through high particle and hardware intertness.

Within our bio series you will discover novel particles, 8 different chemistries, biocompatible hardware, and 24/7 live help with our technical experts.



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The advertisement features a dark, starry background with a colorful nebula. It includes icons for 'Novel Particles' (three blue circles), '8' (a large white number), 'Biocompatible Hardware' (a white syringe), and 'Technical Gurus' (a group of white human figures). A green 'NEW' badge is in the top left, and a 'Learn More' button is at the bottom left.

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