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# TOSOH THE CUSTOMER MAGAZINE

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PANDEMIC/PATIENCE/PEOPLE

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NO. #01 2021

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**TOSOH BIOSCIENCE**

# 02 EDITORIAL DEAR READER

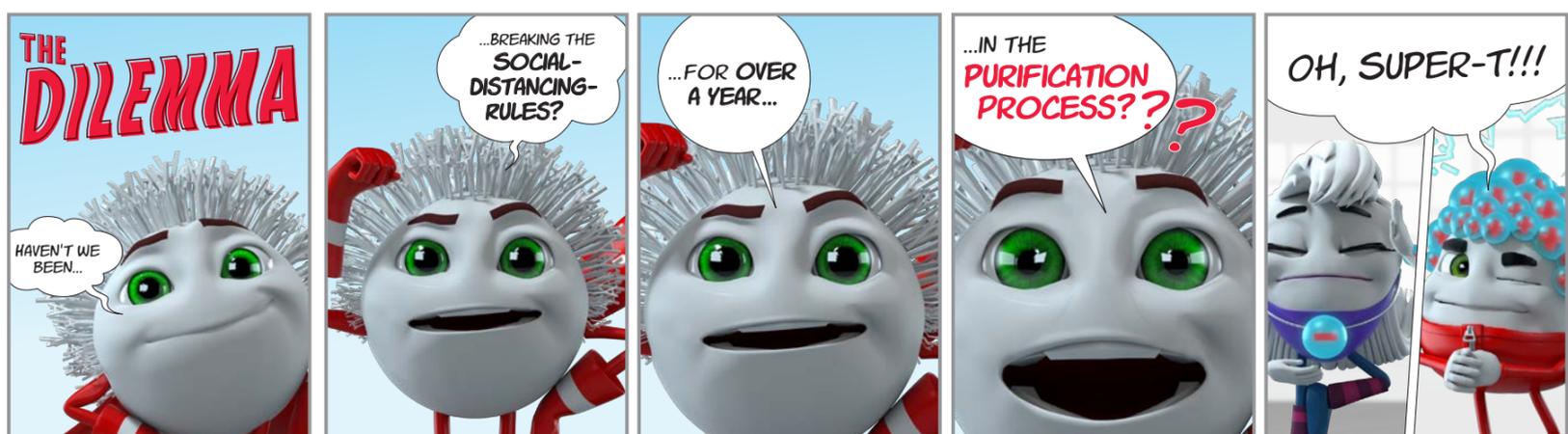
Welcome to the first issue of the Tosoh Bioscience customer magazine in 2021. Writing this editorial feels like watching Groundhog Day: one year later and still working in a pandemic setting. At Tosoh, we are continuing to work remotely and to focus on virtual events such as our new webinar series and the virtual BioSeparation Forum. Your positive feedback encouraged us to create another event: the PolyAnalysis Forum, dedicated to the analysis of natural and synthetic polymers.

Another highlight of this edition is featuring our dedication to work in close cooperation with our Biopharma partners to support their work. Monika Häußler and Birgit Ehrenberg from Rentschler Biopharma share insights into their latest development project and the close cooperation with our chromatography experts..

STAY HEALTHY AND ENJOY READING.

REGINA ROEMLING | SENIOR MARKETING MANAGER  
TOSOH BIOSCIENCE GMBH

## SUPERT, HIS FRIENDS AND THE CORONA RULES



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### ➤ IMPRESSUM

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# 03 WHAT'S NEW COLUMNS

## FCR-IIIa AFFINITY CHROMATOGRAPHY – THE SMART WAY OF GLYCOPROFILING

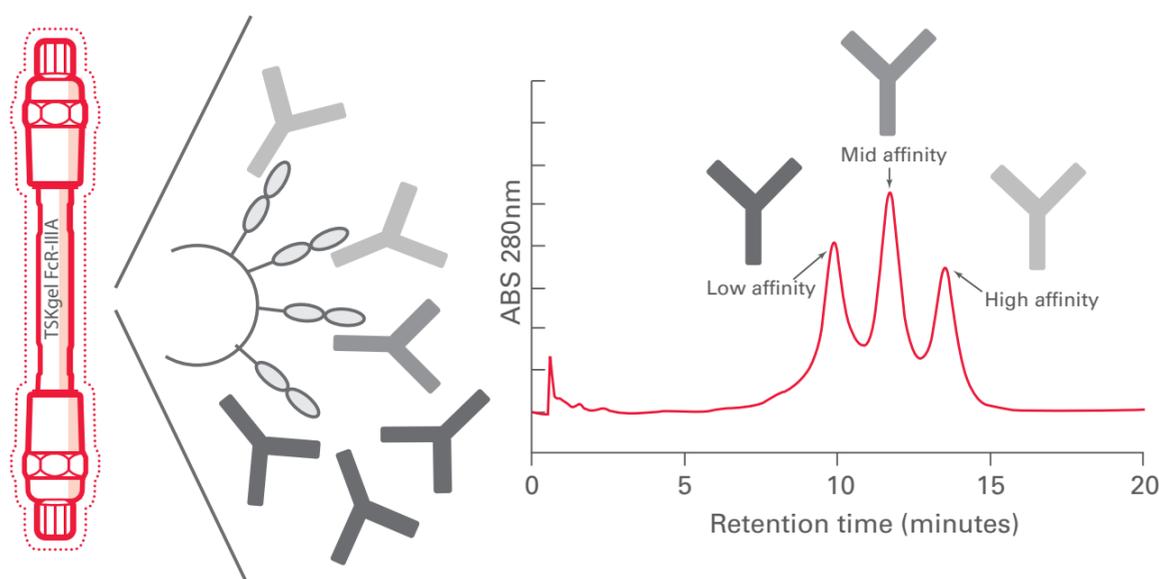
FCR AFFINITY CHROMATOGRAPHY SEPARATES ANTIBODIES BASED ON THE AFFINITY OF THEIR FC REGION FOR A PARTICULAR FC RECEPTOR. IN 2019, WE LAUNCHED TSKgel FcR-IIIa-NPR, A STATIONARY PHASE BASED ON A NOVEL FC GAMMA IIIa LIGAND. THE COLUMN WAS DESIGNED TO QUICKLY ANALYZE THE AFFINITY OF ANTIBODY SAMPLES TO THIS RECEPTOR AND CORRELATE THAT TO MAb GLYCOFORMS. NOW, WE ADDED A NEW, SEMI-PREPARATIVE COLUMN TO THE FCR SERIES ALLOWING COLLECTION OF MAb FRACTIONS ACCORDING TO THEIR FCR AFFINITY.

Fc gamma receptor IIIa (FcγRIIIa) plays a key role in antibody-dependent cell mediated cytotoxicity (ADCC), a crucial mechanism of action of anti-tumor mAbs. The Fc-glycans of antibodies are known to play an important role in Fc-mediated effector functions. The binding of antibodies to FcγRIIIa depends on their glycosylation profile and triggers ADCC in vivo.

TSKgel FcR-IIIa columns separate antibodies based on the affinity of their Fc region for a particular Fc receptor (FcγIIIa) into three fractions. These fractions correlate with different mAb glycoforms and their antibody-dependent cellular cytotoxicity (ADCC) activity. Thus the columns represent a tool to rapidly link FcγIIIa receptor affinity with mAb function and structure.

TSKgel FcR-IIIa-5PW is a semi-preparative affinity column based on a recombinant FcγIIIa receptor ligand bonded to porous 10 μm poly-methacrylate particles. The column can be loaded with up to 5 mg of monoclonal antibody (mAb), allowing material collection in sufficient quantity for in-depth analysis.

The resulting fractions are antibodies of different Fc receptor affinities and can be characterized, for instance as to their glycosylation status, ADCC activity or kinetic binding properties. This helps to understand the basis of Fc receptor affinity, antibody structure and function. Furthermore, data generated with fractions of the FcR-IIIa-5PW column underpin data obtained with FcR-IIIa-NPR column and validate correlations to glycosylation or ADCC.



➤ PRINCIPLE OF FCR AFFINITY CHROMATOGRAPHY

➤ CHECK OUT OUR WEBSITE TO DOWNLOAD VARIOUS APPLICATION NOTES APPLYING FCR AFFINITY CHROMATOGRAPHY.

# 04 EXPERT INSIGHTS

## BIOPHARMA PARTNERSHIPS – A KEY TO SUCCESS

INNOVATORS AT RENTSCHLER BIOPHARMA ARE CONTINUOUSLY DEVELOPING NEW PROCESSES FOR BIOPHARMACEUTICAL PRODUCTION TO TACKLE LIFE-THREATENING DISEASES. WE SAT DOWN WITH DR. BIRGIT EHRENBURG, PROCESS MANAGER, AND MONIKA HÄUSSLER, QUALITY CONTROL (QC) MANAGER, TO DISCUSS ABOUT THEIR LATEST PROJECTS AND HOW CLOSE COLLABORATION WITH OUR CHROMATOGRAPHY EXPERTS HELPED THEM DEVELOP ROBUST, SCALABLE, AND ECONOMICALLY VIABLE DOWNSTREAM PROCESSES, AS WELL AS CORRESPONDING RELIABLE BIO-ANALYTICAL METHODS.

*Tosoh Bioscience (TB):* Monika and Birgit, thank you for sharing your experience with resins and technical support provided by Tosoh. Could you first give us a short summary of your activities at Rentschler Biopharma SE?

Monika Häussler (MH): I am a QC Manager in our quality control development department. We are responsible for the International Council for Harmonization (ICH)-conform establishment, qualification and validation of bioanalytical methods that will later be used for the release of cGMP batches. Our bioanalytical laboratory mostly performs ELISA based methods, such as potency determination of the API or quantification of process-related impurities like host cell proteins (HCP) or Protein L. We also perform quantitative polymerase chain reaction (qPCR) and cell-based assays as well as methods for new API formats such as mRNA-based vaccines.

For our methods, we apply a quality by design approach - a scientific, risk-based approach, focusing on integrating high-quality into a product right from the beginning. Furthermore, we are constantly implementing new state-of-the-art methods and products into our portfolio, such as the aforementioned mRNA-based vaccines.

Birgit Ehrenberg (BEE): I am a process manager in the MSAT (Manufacturing Science & Technology) team. I oversee DSP processes and chaperone client Active Pharmaceutical Ingredient (APIs) throughout the complete product life cycle. We always aim to develop robust, scalable, and economically viable downstream processes. This includes the design and documentation of the process qualification and validation at manufacturing scale within demanding clinical and commercial timelines. Additionally, we establish control strategies and continued process verification to ensure the highest quality.



➤ DR. BIRGIT EHRENBURG



➤ MONIKA HÄUSSLER

*TB:* Birgit, you decided to evaluate some innovative resins from Tosoh Bioscience lately. What was the trigger to test something new?

BEE: TOYOPEARL® Sulfate-650F demonstrated superior polishing capabilities during the process development for a new designer molecule. These properties were not provided by other conventional cation exchange resins that were tested in parallel. The resin demonstrated sufficient protein binding capacity at elevated ion strength while removing aggregates in bind-elute mode, accomplishing 98% or higher monomer content as determined by HPLC.

Additionally, the different and unique selectivity of TOYOPEARL® NH<sub>2</sub>-750F was evaluated during the polishing step in the purification process of yet another designer molecule. Not only did it demonstrate sufficient high protein binding capacity at elevated ion strength, but it was also successful in removing aggregates in bind-elute mode at a pH close to its isoelectric point.

# 05 EXPERT INSIGHTS

## BIOPHARMA PARTNERSHIPS – A KEY TO SUCCESS

*TB: Did you face some challenges during the evaluation? What helped you learn how to work with those newer chromatography media?*

BEE: Yes, during evaluation we quickly realized that buffer fine-tuning would be necessary to optimize aggregate removal. To this end, we optimized conditions to develop a robust process step. Tosoh's customer support and a published Application Note aided us in our decision-making progress by providing relevant information.

*TB: Monika, you implemented a Protein L ELISA test in your analytical toolbox. How did Tosoh support you in this journey?*

MH: Tosoh made three of their Protein L-T36 Kits available to us for testing, free-of-charge. During testing, we aimed to build on our existing know-how and experience in order to give feedback for potential improvements for the kits. Tosoh accepted our suggestions and implemented these in a timely manner. We were also offered an advantage from the logistics perspective as delivery time of the kits was shortened by stocking up on some kits in Europe, thereby circumventing shipment from Japan.

*TB: What is mandatory for you to implement a new resin or analytical technique in your processes?*

MH: Reliability is a key factor while making this decision. In addition to that, other factors such as the guaranteed delivery of reagents and materials of consistently high quality over a longer time period is essential.

BEE: From the implementation point of view - in addition to the Certificate of Analysis - we also appreciate detailed Regulatory Support Files (RSF) in case of product contact. This is important for the extraction of the data supporting pharmaceutical toxicology evaluation or sanitization options.

*TB: You were both in regular contact with Tosoh chromatography experts during your development and implementation work. How would you describe the collaboration?*

MH: The collaboration with Tosoh was very pleasant and professional. We were always supported in a friendly, open-minded, interactive, supportive, and prompt manner.

BEE: The Tosoh Bioscience product quality, customer service and fast supply chain ensured a very productive collaboration. Additionally, support was extended immediately by a very knowledgeable technical team. I would like to take this opportunity to thank Tosoh for its professional expertise.

BEE: One always strives for accelerating processes while improving product quality, and to this end, novel approaches that can provide these results are a good match for us.

*TB: Are you missing anything when it comes to developing new purification or analytical methods?*

MH: Working with new molecules and formats means having to continuously improvise and innovate. In general, higher throughput with optimum efficiency could be facilitated by the increased incorporation of automation through the usage of minimum material and closer linkage between the analytics and purification steps.

*TB: Which changes do you expect to happen in the Biopharmaceutical Industry and more specifically in Downstream Processing and Biomolecule Analytics?*

MH: The biopharmaceutical industry has always been very innovative and will certainly come up with many new targets and products in the near future. A good example for this is mRNA-based biopharmaceuticals that are relatively new to the market. The analytical industry has to be equally innovative to foster and support the growth of these new modalities. This will be vital in ensuring high product quality and patient safety.

BEE: Complex biomolecules demand an increasing flexibility of all parties involved. A continued modular and versatile capacity management along the supply chain will be extremely significant in the years to come. In addition, a supportive IT landscape for just-in-time-delivery and growing databases for rapid communication will be key to translating scientific research into outstanding biopharmaceuticals.

As biopharmaceutical formats grow more complex, it is important that downstream processing and biomolecule analytics keep pace to ensure the highest quality. This is of utmost importance to our work here at Rentschler Biopharma.

*TB: Birgit and Monika, thank you very much for sharing these insights*



➤ RENTSCHLER BIOPHARMA HEADQUARTERS AT LAUPHEIM, GERMANY

# 06 PEOPLE BEHIND TOSOH

## MAURICE DIWO, TOSOH BIOSCIENCE GMBH, GRIESHEIM, GERMANY

**MAURICE JOINED THE SALES TEAM OF TOSOH BIOSCIENCE LAST SUMMER. MOST OF THE ONBOARDING AND TRAINING WAS PERFORMED REMOTELY DUE TO THE PANDEMIC.**

*Tosoh Bioscience (TB): Maurice, you joined Tosoh Bioscience some months ago. How did you get to know about Tosoh?*

Maurice Diwo (MD): During my time as a doctoral student at the Helmholtz-Centre for Infection Research in Braunschweig, I had already done a lot of chromatography work, but I did not use Tosoh products there. When I was at an advanced stage of my PhD and slowly started to look at the job market I became aware of Tosoh through a recruiting agency. The first contact I had was with the sales team, but then very soon with marketing and the tech team, as well.

*TB: Could you please tell our readers a little bit about yourself and what you do for Tosoh?*

MD: I joined the sales team of Tosoh Bioscience last summer as Technical Sales Specialist. I take care of our customers in the south of Germany as well as in Switzerland. Of course, I originally planned to visit our customers personally, but the current pandemic has also changed our way of working a lot. So currently I mainly advise users via video telephony or emails. During my PhD, I isolated high molecular weight protein complexes and characterized them by means of structural biology, biophysics and biochemistry. I think that this gathered experience is now very beneficial to me and that I can quickly put myself in the shoes of our customers.

*TB: What motivated you to switch from academia to industry?*

MD: I did not make the decision easily. It is part of my personality to get to the bottom of complex issues and to want to understand their interrelationships in detail. It's very important to me to live out this characteristic in my job, too, and I can do that in technical customer consulting, for example. What attracted me to a career in industry, however, was the long-term security of employment and the broad opportunities for further training and development. It was time to start building up new experience.

*TB: What part of the work do you like most?*

There are several aspects to this. First, of course, there are the large projects, which require a lot of coordination between several parties and good teamwork. When a large delivery is completed, I find it very rewarding. On the other hand, I still have a lot of fun poring over details and being able to offer the optimum product from our range for a particular problem.

*TB: What were the highlights during your first months at Tosoh?*

My highlights were the great reception in the team and the really well-structured training. The entire team went to great lengths to ensure that the on-boarding phase was successful despite the special circumstances. So I felt at home in the team very quickly.

*TB: What are your interests besides Chromatography?*

I love to travel and most of all I like to combine getting to know cultures together with their cuisines. So it has almost become a ritual for me to attend cooking classes when visiting a foreign country. This way I can recall the memory of something I experienced by having a delicious dinner when I get back home. And if the relaxation should take place without calorie intake, I spend the time in front of one of my aquariums and watch our dwarf-shrimps, preferably together with my little daughter. I think it's great to recreate a piece of nature in your own home.



➤ DISHES FROM ALL OVER THE WORLD



➤ MAURICE AT WORK

# 07 PEOPLE BEHIND TOSOH

## SÉBASTIEN, TELL US MORE ABOUT LIGHT SCATTERING

**SÉBASTIEN ROUZEAU, OUR PRODUCT MANAGER FOR GEL PERMEATION/SIZE EXCLUSION CHROMATOGRAPHY (GPC/SEC) WAS PART OF THE TEAM THAT DEVELOPED THE NEW LenS3 MALS DETECTOR. WE ASKED SÉBASTIEN TO INTRODUCE US TO THIS NEW APPROACH TO LIGHT SCATTERING.**

*Tosoh Bioscience (TB): Sébastien, what is light scattering?*

Sébastien Rouzeau (SR): Light scattering can be described using a situation familiar to most of us: driving in the fog at night. A car's headlights illuminate droplets in the fog, which re-emits light in all directions. As a result, we can see the fog from wherever we stand, even from behind the car. In analytical detectors, a laser beam is used to illuminate a cell that contains a sample in solution. The intensity of scattered light is related to the molecular weight of the sample. However, that intensity is not equal in all directions; it changes with the angle of observation, and this scattering pattern is related to the size of the sample. Light scattering relates to both molecular weight and size.

*TB: Why has light scattering become so popular for polymer and protein characterization?*

SR: Light scattering is primarily used to determine the true or absolute molecular weight of a sample. Size information can be obtained in the form of the radius of gyration ( $R_g$ ), which is truly related to the shape and the structure of the molecule. Light scattering is most often coupled with size exclusion chromatography (SEC), known as SEC-multiangle light scattering (SEC-MALS). Monomers, multimers, or higher aggregates and fragments can be easily identified for protein applications, regardless of their shape. For polymer characterization, light scattering is mostly used to look into the molecular weight distribution. And it is also possible to obtain valuable information on the structure or the confirmation of the sample (e.g. branching).

*TB: Are there any limitations to light scattering measurements?*

Essentially, light scattering instruments either measure as close to the incident beam as possible to obtain molecular weight, or measure at multiple angles (the MALS approach) to observe how the intensity changes and extrapolate back to  $0^\circ$  to estimate molecular weight. Like any analytical technique, MALS has its limitations, some of which are related to the instrument design: One is related to the lowest and highest measurable angles of traditional MALS detectors. This is due to the cell geometry and the limited space to fit the photodiodes around it. The extreme angles are subject to higher background noise because of the proximity of the incident laser beam and stray light. This is an issue because the lowest angle is extremely critical to obtain an accurate molecular weight and the highest angle is very important when it comes to detecting very small differences in scattering for small samples. This is basically the reason why the lower limit for  $R_g$  measurements by a traditional MALS detector is approximately 10–12 nm.

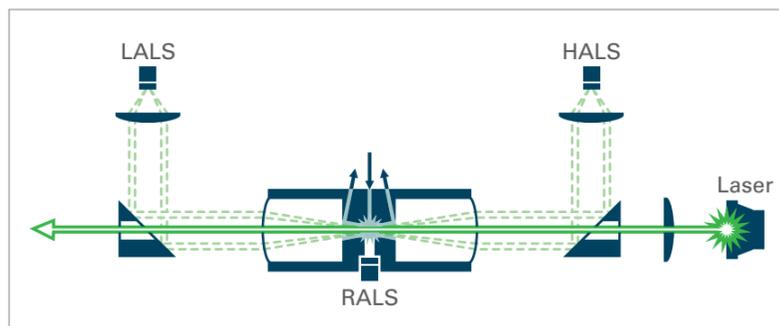
*TB: How does the new LenS3 MALS detector address such limitations?*

SR: One of the key features developed to overcome these limitations is the completely new concept of using a "flow channel" instead of the traditional flow cell: an elongated flow path with a dual-cone shape machined in a black polymeric material. The block is sealed with two lenses which will let the laser beam go through the channel to illuminate the sample while ensuring the collection of scattered light at an ultralow and ultrahigh angle. There is also a third angle that collects light at  $90^\circ$  to form a three-angle measurement.

This new design features two major benefits: First, the black polymeric material eliminates any stray light that could interfere with the scattered light and generate noise. Second, the elongated flow path maximizes the interaction with the sample and significantly increases the amount of light that can be collected. In addition, we use a green laser that produces about three times higher intensity of scattered light than a regular red laser. Overall, what sets this instrument apart from others is twofold: the position of the angles - with a true usable low angle for direct molecular weight measurement, combined with an extreme high angle for  $R_g$  measurement - and the new flow channel and optics that maximize the signal-to-noise to increase the overall sensitivity.

*TB: What does this mean for SEC-MALS users?*

SR: The higher sensitivity brings about various benefits for users: The LenS3 requires smaller quantities to characterize samples, important especially for biomolecule applications. Additionally, the high sensitivity combined with the position of the extreme angles opens a whole new field of application for small macromolecules with an  $R_g$  below 10 nm because the angular dissymmetry can be measured for such small sizes, which was not possible before.



➤ THE REVOLUTIONARY OPTICS DESIGN OF LenS3 MALS DETECTOR

# 08 WHAT'S HAPPENING TOSOH TUESDAY

## A NEW WEBINAR SERIES FEATURING #CHROMATOGRAPHY EXPERTS

BASED ON THE SUCCESS OF OUR VIRTUAL WORKSHOPS, WE HAVE OPENED YET ANOTHER DIGITAL CHANNEL TO STAY IN TOUCH WITH USERS OF CHROMATOGRAPHY PRODUCTS – THE TOSOH TUESDAYS. ONCE A MONTH, OUR DIRECTOR SALES & MARKETING, CHRISTIAN ROHRER, INVITES CHROMATOGRAPHY EXPERTS TO TALK ABOUT A DEDICATED TOPIC.

The Tosoh Tuesday webinars started in December 2020 and cover a broad choice of chromatographic topics in a compact format. Alternating guests, each an expert in their own field, present current trends, new technologies or specific applications related to liquid chromatography in a 30-minute lecture followed by a short Q&A session.

In the meantime, the first issues of our Tosoh Tuesday webinar series have been broadcasted and are available on our #chromatography experts channel on demand. Topics covered are UHPLC analysis of biopharmaceuticals, efficient purification of biomolecules, enhanced GPC/SEC analysis, cost reduction of Protein L capture steps, glycosylation analysis of antibodies and packing of large process columns. The next webinar will take place on June 15 with a focus on using light scattering detection in practice.



CHECK OUT OUR WEBINARS ON DEMAND HERE:

[HTTPS://WWW.GOTOSTAGE.COM/CHANNEL/CHROMATOGRAPHYEXPERTS](https://www.gotostage.com/channel/chromatographyexperts)

## NEWS & EVENTS | MEET TOSOH BIOSCIENCE IN THE VIRTUAL WORLD

### UPCOMING EVENTS

MANY LIVE EVENTS IN 2021 ARE ALREADY CANCELLED OR POSTPONED TO 2022. NEVERTHELESS, SOME EVENTS ARE STILL ANNOUNCED FOR AUTUMN AND WINTER 2021  
➤ AND YOU CAN FIND THE LATEST UPDATES HERRE [WWW.SEPARATIONS.EU.TOSOHBIOSCIENCE.COM/NEWS-EVENTS/EVENTS](http://WWW.SEPARATIONS.EU.TOSOHBIOSCIENCE.COM/NEWS-EVENTS/EVENTS)

- JUNE 15 | 2021 ➤ TOSOH TUESDAY – GPC/SEC-MALS IN PRACTICE, WEBINAR
- JUNE 17 | 2021 ➤ BIOSEPARATION FORUM – NEW ANTIBODY MODALITIES, DIGITAL
- SEPT 5 - 8 | 2021 ➤ RDPA, RECENT DEVELOPMENT IN PHARMACEUTICAL ANALYSIS, DIGITAL
- SEPT 22 - 23 | 2021 ➤ OLIGONUCLEOTIDE DISCOVERY AND DELIVERY 2021, LONDON [UK]
- OCT 18 - 20 | 2021 ➤ IOPC, INTERNATIONAL OLIGONUCLEOTIDES & PEPTIDES CONFERENCE, DIGITAL
- OCT 19 - 21 | 2021 ➤ ILMAC 2021, BASEL [SWITZERLAND]

IN ADDITION, WE RECOMMEND THE VARIOUS RESOURCES THAT WE PROVIDE ON OUR WEBSITE, OUR SOCIAL MEDIA AND ON OUR  
➤ YOUTUBE CHANNELS: [HTTPS://WWW.YOUTUBE.COM/CHANNEL/UC5FRZ1W7AP8DIVZCGLZLWKW](https://www.youtube.com/channel/UC5FRZ1W7AP8DIVZCGLZLWKW)