TOSOH

TOSOH
THE CUSTOMER
MAGAZINE

NO.#01
2019

FACTS/FUN/FC RECEPTOR

TOSOH THE ART OF SEPARATION

TOSOH BIOSCIENCE

02
EDITORIAL
DEAR READER

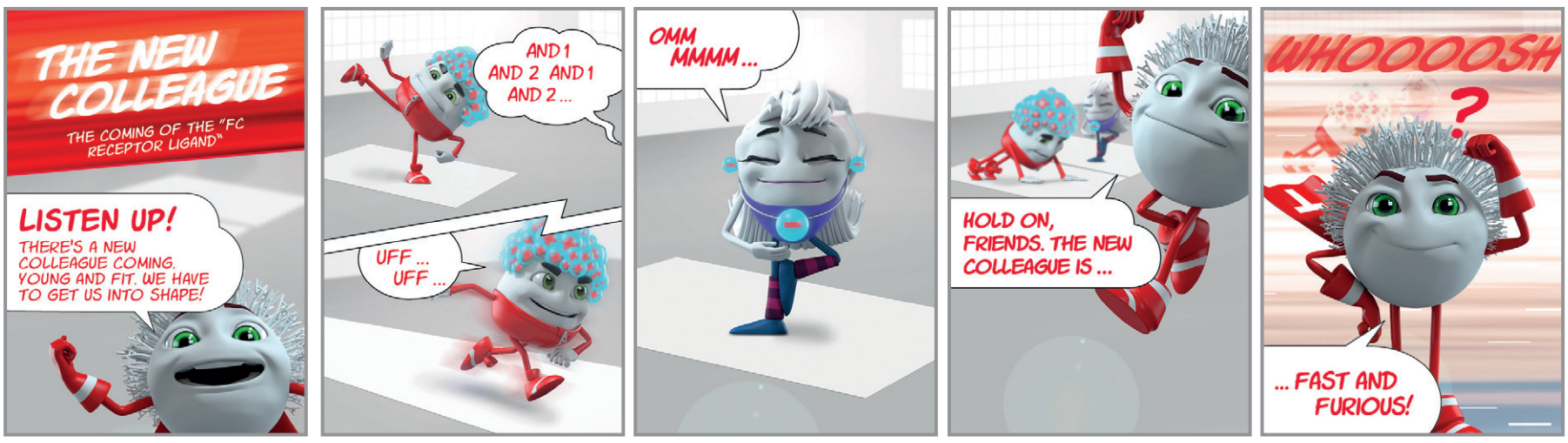
Welcome to the first issue of the Tosoh Bioscience customer magazine in 2019. The motto of this issue is Facts/Fun/Fc Receptor. Our spring highlight with regard to HPLC is the release of the Fc receptor affinity column TSKgel FcR-IIIA-NPR, that offers a new approach to quickly assess ADCC activity of antibodies.

We also take a look back at our conference event, the HIC/DSP Bioseparation Conference, which was held in the Alps, in Interlaken, Switzerland. About 100 participants enjoyed lively scientific discussions in a beautiful winter surrounding. We are looking forward to meeting you in June at the HPLC 2019 Conference in Milan, Italy and enjoying more separation science.

ENJOY READING AND STAY INFORMED.

REGINA ROEMLING | SENIOR MARKETING MANAGER
TOSOH BIOSCIENCE GMBH

THE SUPER-T - COMIC #9



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IMPRESSUM

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03 WHAT'S NEW COLUMNS

TSKgel FCR-IIIA-NPR: A NEW APPROACH TO ASSESS ADCC ACTIVITY

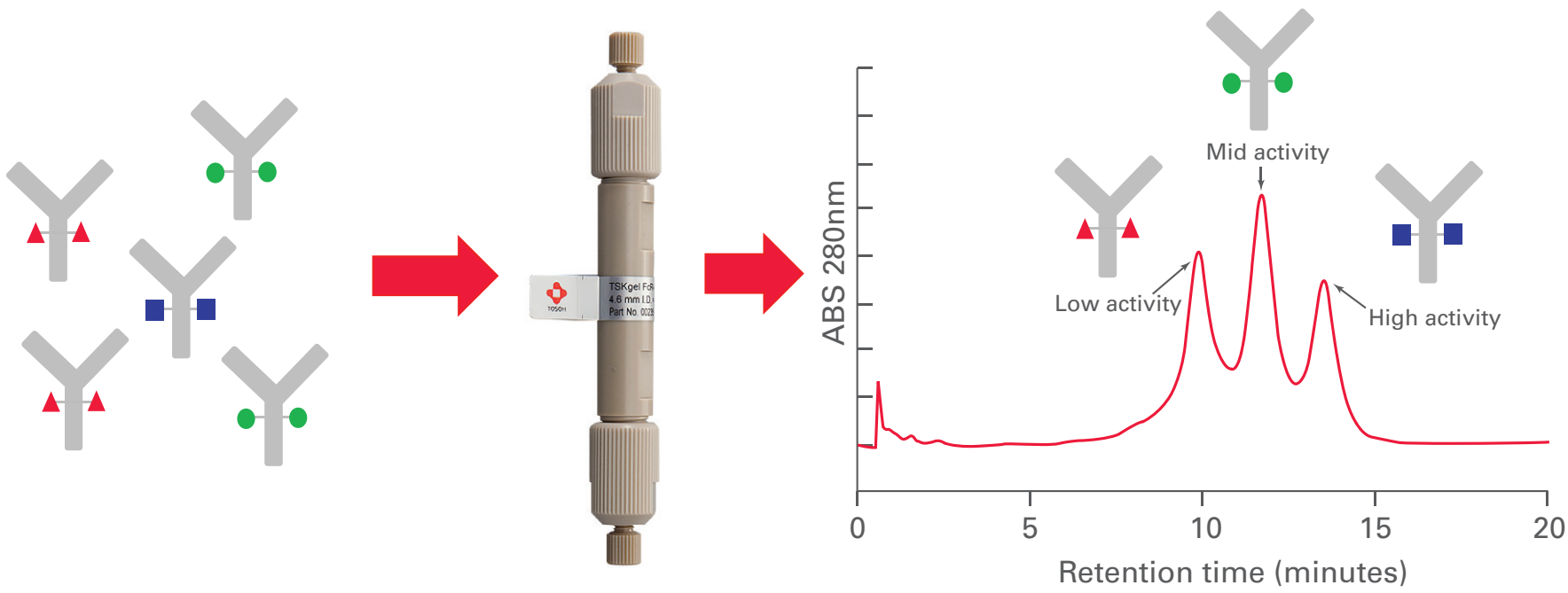
IN FEBRUARY, WE INTRODUCED TSKgel FCR-IIIA-NPR, A NEW HPLC AFFINITY COLUMN BASED ON THE RECOMBINANT FCγIIIA RECEPTOR - A KEY PLAYER IN ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY (ADCC). FCγRIIIA AFFINITY CHROMATOGRAPHY ALLOWS FAST EVALUATION OF BIOLOGIC ACTIVITY AND GLYCOFORM PATTERNS OF ANTIBODIES. THIS INNOVATIVE AND ROBUST METHOD CAN PROVIDE VALUABLE INFORMATION DURING CELL LINE SELECTION, UPSTREAM OPTIMIZATION, OR QUALITY CONTROL OF THERAPEUTIC ANTIBODIES.

Antibody-dependent cell-mediated cytotoxicity (ADCC) is an important mechanism of action (MoA) of monoclonal antibodies used in cancer treatment. Selecting suitable cell lines and optimizing culture conditions towards expression of antibody candidates with desired ADCC activity is an essential part of the R&D process. A fast and straight forward approach to easily access ADCC activity would facilitate screening of a large number of clones or monitoring the effect of upstream process variations. FCγIIIa receptor plays a key role in the ADCC process by interacting with the N-glycans of IgG Fc regions.

Our new HPLC column uses a recombinant Fc receptor as ligand for affinity chromatography to deliver valuable information about expected ADCC activity and mAb glycoform distribution. Glycoforms of an antibody sample can be partly separated based on the strength of their binding to the FcR ligand. Resulting peaks can be assigned to low, medium, and high ADCC activity (Figure 1). Separation patterns can be correlated to Fc N-glycans. Terminal galactose residues increase affinity to TSKgel FcR-IIIA-NPR while core fucose residues reduce it. This correlates with the known influence of galactose and fucose on ADCC activity.

This rapid thirty minute separation allows the analysis of large numbers of mAb samples to gain valuable initial information on the distribution of glycoforms and expected ADCC activity. This efficient method can be applied to purified samples and supernatant alike and can therefore be used in many phases of development and production such as cell line screening in early R&D, biosimilar/originator comparison, upstream development and optimization, monitoring of glycoengineering, or lot comparison.

In March, this ground-breaking new technology was awarded one of the Pittcon Today Excellence Silver Awards for ingenuity and creativity in scientific advancement. The Pittcon Awards were designed to recognize innovations at the Pittcon Exhibition. A panel of judges – consisting of thought leaders from across academia, industry and trade media – viewed all types of scientific innovations and selected the winners based on submissions' ingenuity, creativity, implementation and outcomes, as well as the products' projected impact on the industry.



FcR AFFINITY CHROMATOGRAPHY

FOR MORE INFORMATION HTTPS://WWW.SEPARATIONS.EU.TOSOHBIOSCIENCE.COM/SOLUTIONS/HPLC-PRODUCTS/AFFINITY/TSKGEL-FCR-LLLA-NPR-E

04 CONFERENCE REVIEW

11TH HIC/DSP BIOSEPARATION CONFERENCE IN INTERLAKEN, SWITZERLAND

THE 11TH EDITION OF THE HIC/DSP BIOSEPARATION CONFERENCE (FORMERLY KNOWN AS HIC/RPC) TOOK PLACE ON FEBRUARY 18-21, 2019 IN INTERLAKEN, SWITZERLAND. THIS LATEST OCCURRENCE KEPT AN EYE ON THE HIC FUNDAMENTALS WHILE EXPANDING ITS SCOPE TO ALL MODES OF CHROMATOGRAPHY, FOCUSING MORE ON THE OUTPUT OF SEPARATION TECHNIQUES IN DOWNSTREAM PROCESSING (DSP): THE EFFICIENT PURIFICATION OF BIOMOLECULES.

The conference venue was a stunning Art Nouveau hall at the Hotel Royal-St Georges in Interlaken. Interlaken is located between Lake Thun and Lake Brienz, close to famous Swiss winter holiday spots, such as Wengen or Grindelwald. It is surmounted by the three famous mountains Eiger, Mönch and Jungfrau. The beautiful venue and winter surrounding of the Conference combined with an excellent scientific program created the ideal atmosphere to encourage the exchange of ideas and thoughts among the attendees.

Today's most challenging elements of modern downstream processing are the continuous increase in expression levels in fermentation and cell culture, the stringent demands for purity and recovery of biopharmaceuticals, and the highly competitive environment. The conference presenters and attendees discussed potential solutions for these problems using new chromatography media and innovative processes.

Roman Necina (Takeda, Austria) gave the first industry keynote lecture right after the opening remarks by Shigeru Nakatani, the managing director of Tosoh Bioscience, Germany and Alois Jungbauer, Professor at the University of Natural Resources and Life Sciences, Austria, and chairman of the conference. Roman emphasized the impact of complex biopharmaceuticals in the development and implementation of novel technologies and manufacturing equipment, automated online assays, and data science.

Klaus Graumann (Phoenestra, Austria) opened the second day of the conference with the second industry keynote lecture on trends in development and manufacturing in the biopharma industry. Stefan Hepbildiker (Roche, Germany) gave the third and last industry keynote lecture. He focused his talk on how bioprocess development can balance innovation in therapeutic modalities, speed, cost, and patient safety.

The talks in the plenary sessions were well balanced between practical elements of chromatographic development and implementation, theoretical fundamentals and mechanistic approaches, and novel strategies and theories. Within these sessions, chromatography experts from Tosoh Bioscience shared their visions and achievements in several talks and multiple posters. Egbert Müller (Germany) reported the influence of the hydrophobicity of the payload on resolution and recovery of ADCs in HIC chromatography. Patrick Endres (Germany) analyzed the critical quality attributes in continuous Protein A chromatography. Bill Evans (USA) explained how to improve operational productivity in Protein A chromatography by optimizing column dimensions. Toru Tanaka (Japan) presented the latest results obtained with the groundbreaking FcγRIIIA affinity chromatography for fast evaluation of ADCC activity.

THE SCIENTIFIC COMMITTEE; FROM LEFT TO RIGHT: ARNE STABY, ALOIS JUNGBAUER, EGBERT MÜLLER, TODD PRZYBYCIEN, CRISTINA DIAS-CABRAL, ALEXANDER FAUDE, AND RON BATES

05 CONFERENCE REVIEW

A traditional and expected moment of the HIC/DSP Conference is the panel discussion. Ron Bates and Arne Staby lead this year's edition after collecting questions and suggestions from the audience. The use of continuous chromatography from a GMP point of view, the feasibility of platform processes for non-mAb biomolecules, and the hurdles for process optimizations post-filing / approval were discussed heavily during the 2-hour session.

The academic poster presenters had the opportunity to present their work on stage. Todd Przybycien helped them to deliver the best message in the 5-minute slot they had. All poster presenters had time during the Poster Apero Session to discuss their results and achievements with the attendees. The use of electronic poster screens was critically acclaimed and accounted for more in-depth discussions.

A great benefit of spending several days with the most prominent scientists and professionals in the DSP world is the tremendous amount of information exchanged between all the participants. To support this, specific networking times and exciting social activities rounded up the week in Interlaken. The excursion to Jungfraujoch - Top of Europe on the second day of the conference was a highlight for all participants!

To wrap-up this 11th HIC/DSP Bioseparation Conference, we will only quote the closing remarks from Alois Jungbauer: "The engagement of Tosoh Bioscience as the sponsor of this conference goes way beyond marketing. Tosoh demonstrated a dedication to supporting the scientific and technical development of Downstream Processing."

PICTURE 1: **CHAIRMAN ALOIS JUNGBAUER**

PICTURE 2: **LIVELY DISCUSSIONS AFTER EVERY TALK**

GROUP PICTURE AT THE JUNGFRAUJOCH

06
WHAT'S NEW
GPC TECHNOLOGY

INNOVATIVE GPC INSTRUMENT TECHNOLOGY ON THE HORIZON

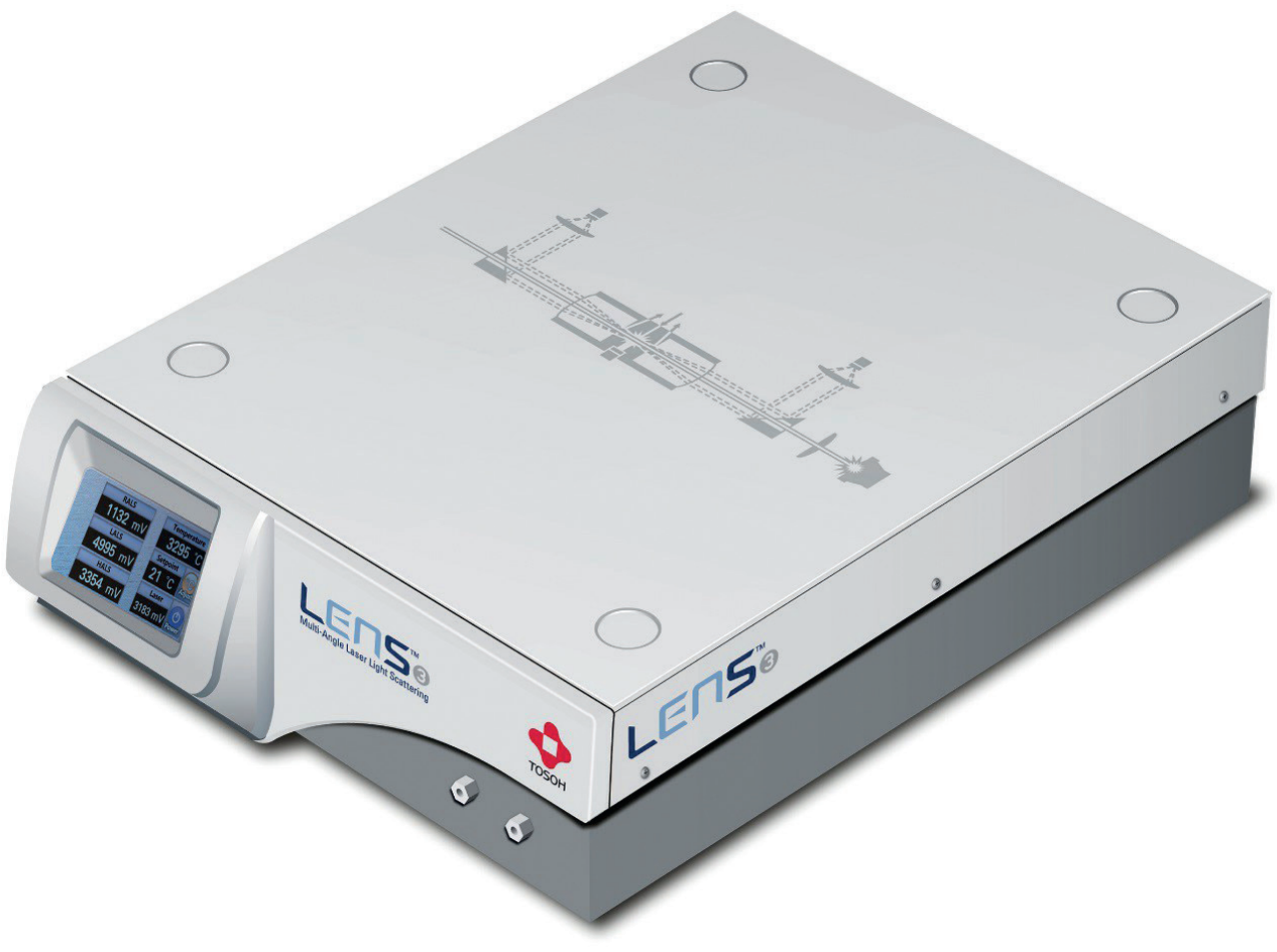
THIS YEAR WILL SEE TWO IMPORTANT ADDITIONS TO OUR SEC/GPC PRODUCT LINE: THE NEW EcoSEC ELITE, THE SUCCESSOR OF OUR WELL KNOWN AMBIENT EcoSEC SYSTEM, AND THE MOST PROFOUND INNOVATION IN LIGHT SCATTERING TECHNOLOGY IN DECADES, THE LenS3 MALS DETECTOR.

The LenS3 MALS Detector is the most profound innovation in light scattering technology in decades. The new detector integrates the best of both Multi-Angle and Low-Angle Light Scattering (MALS and LALS) concepts to create a new paradigm in light scattering detection. By combining an extreme low angle (LALS – 10°) and an extreme high angle (HALS – 170°) with a right angle (RALS – 90°) to form a 3-Angle MALS detector (10° + 90° + 170°), LenS3 is capable to determine absolute molecular weight directly, using LALS in its purest form, and measure angular dependence using MALS to calculate Radius of Gyration, Rg.

As opposed to a conventional flow cell, the new detector employs a patent-pending extended "flow chamber", allowing maximum interaction of the incident beam with the molecules of interest resulting in significantly higher scattering intensity. Coupling this unique design feature with a lower laser wavelength, 514 nm as opposed to a typical 660 nm, LenS3 sets a new benchmark in detection sensitivity unmatched by any such commercial Instrument.

The LenS3 is supported by a new and improved patent-pending angular dependence calculations using the "Angular Dissymmetry Plot" that allows the measurement of Radius of Gyration without the need for solution concentration and refractive index increment (dn/dc) values. Thanks to the new theory, the strategic positions of the angles, and superior sensitivity, LenS3 can now detect angular dependence (or angular dissymmetry) and determine Radius of Gyration values at much lower size range compared to existing MALS instruments with many more angles of observation.

This summer, the EcoSEC Elite SEC/GPC system will replace the current EcoSEC system. This next generation high performance GPC system delivers greater stability and reproducibility than ever before. EcoSEC Elite is an integrated GPC system equipped with the functional instrumentation necessary for accurate analysis of molar mass distributions. Every unit has been updated including the pump unit, degasser unit, and column oven to achieve excellent stability and reproducibility. When used together with options such as a solvent stocker and temperature-controlled sampler table unit, the system further improves baseline stability and supports the measurement of samples over time.



07
PEOPLE BEHIND TOSOH

DR. ELKE PROHASKA, TOSOH BIOSCIENCE GMBH, GRIESHEIM, GERMANY

END OF MARCH, ELKE PROHASKA, SALES MANAGER PROCESS BUSINESS EMEA, HAS LEFT TOSOH BIOSCIENCE AT HER OWN REQUEST INTO RETIREMENT. ELKE JOINED TOSOH IN SEPTEMBER 2003 AS A BUSINESS DEVELOPMENT SPECIALIST, RESPONSIBLE FOR BAVARIA, AUSTRIA AND SWITZERLAND. LATER EASTERN GERMANY AND HUNGARY WERE ADDED TO HER TERRITORY. SHE WAS THEN PROMOTED TO BUSINESS DEVELOPMENT MANAGER AND SINCE 2010 SHE HEADED THE PROCESS BUSINESS SALES GROUP AS SALES MANAGER PROCESS BUSINESS, EMEA. DURING HER LAST SALES MEETING WE TOOK THE OPPORTUNITY TO HAVE A CHAT WITH ELKE AND REVIEW HER TIME WITH TOSOH.

Tosoh Bioscience (TB): How did the biopharmaceutical industry develop during the last 15 years?
Elke Prohaska (EP): In general, the Biotech and Biopharma market experienced an impressive growth. When I started, the main types of biopharmaceuticals were insulin, growth hormones and blood factors. Monoclonal antibodies started to become more and more important. Key targets of today are biosimilars and antibody constructs (bispecific and other fusions). The "new therapies" like gene therapy and cell therapy are starting off right now.
With regard to manufacturing technology, disposables and prepacked columns are getting very popular to reduce investment costs and increase flexibility of manufacturing. Production is developing from large cultures in stainless steel to smaller scales and more variable and flexible approaches.

TB: In your opinion, how has Tosoh changed in the past fifteen years?
EP: Tosoh Bioscience GmbH faced some major changes: shared services such as customer service, human resources, accounting were centralized in the Belgian headquarters and in 2014 our office moved from Stuttgart to Griesheim in the Rhein-Main area. With regards to chromatography products, we introduced the Tosoh GPC instruments in Europe and Tosoh Corporation continuously developed exciting new UHPLC columns and chromatography resins. Especially the new salt tolerant ion exchange media and new affinity ligands like the recombinant Fc receptor stand out from the competition. The production capacity for resins in Japan was almost tripled during my time with Tosoh.

TB: What did you like most in your job?
EP: I loved the personal interaction with scientists, colleagues and users from many countries with different cultural background. During the various positions at Tosoh I got an insight into many different companies and research institutes and I really enjoyed the exchange of ideas with my customers and the scientific discussions at conferences.

TB: Do you remember a very special moment or experience?
EP: My trip to Japan to visit our headquarters in Tokyo and the Nanyo factory in Yamaguchi was the absolute highlight. I was impressed by the extraordinary friendliness of the people. Other great experiences were the seminars I gave together with our distributors in Israel and Turkey.

TB: Now that you leave your job in biotech, will you miss something?
EP: I made a lot of friends during my work life and hope to stay in contact. I may even miss the compulsion to keep moving out of my comfort zone.

TB: What are your plans for the future?
EP: The desire to spend more time with my partner and family was the main reason for retiring early. We plan to travel a lot, do bio gardening and to further renovate our weekend cottage. I have always done a lot of sports and would like to intensify that again.

TB: Elke, Thank you very much for being such a great colleague and all the best for the future!

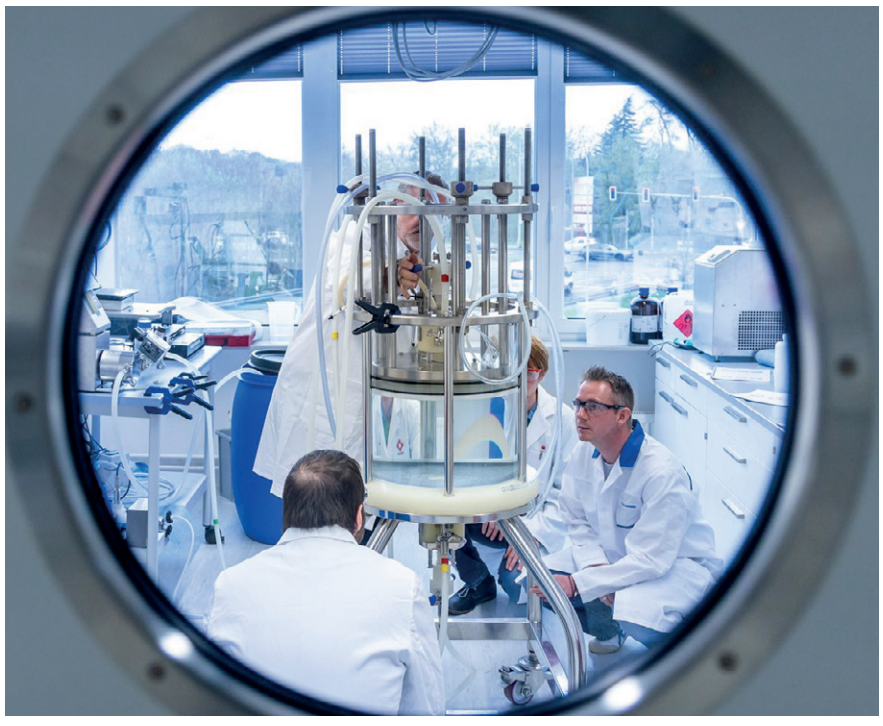
AT CUSTOMER VISIT IN 2007

GOOD BYE ELKE!

08
WHAT'S HAPPENING
WORKSHOPS

TRAINING COURSES IN THE TOSOH BIOSCIENCE OFFICE IN GRIESHEIM

IN 2019 THE CALENDAR OF TOSOH WORKSHOPS AND TRAINING COURSES IS TIGHTLY PACKED WITH EXCITING EVENTS. BESIDES HOSTING THE HIC/DSP CONFERENCE IN INTERLAKEN IN FEBRUARY WE ALSO CONDUCTED OUR 3-DAY GERMAN TRAINING COURSES ON CHROMATOGRAPHY IN PROCESS DEVELOPMENT AND PRODUCTION FOR THE FIRST TIME IN OUR OFFICE IN GRIESHEIM, RECENTLY.



HANDS ON TRAINING IN THE LAB

The popular workshops that have been held for over twenty years provide a comprehensive background to chromatographic purification in bioprocessing. Up to 12 attendees per course gather experience in how process method development translates into a productive and cost effective manufacturing process. The program of these courses offer a balance of presentations and practical hands-on experience under the guidance of qualified tutors.

Topics range from basics of common chromatographic modes, packing chromatography columns, strategies of process development to tips and tricks for cleaning chromatography media in place. The practical part covers various aspects: packing of axial and radial chromatography columns in laboratory and pilot scale, robotic screening and method development, and scale-up of a chromatographic separation.

The new venue was enthusiastically received by the attendees, who also appreciated the insight into our office in Griesheim and the close contact to the whole Tosoh Bioscience team there.

NEWS & EVENTS | MEET TOSOH BIOSCIENCE

MEET TOSOH AT TRADESHOWS AND CONFERENCES

UPCOMING EVENTS

JUNE	16 - 20	2019	HPLC 2019 | MILAN	[ITALY]
SEPT	8 - 11	2019	RDPA 2019 | PESCARA	[ITALY]
SEPT	23 - 24	2019	BIOTALK 2019 | BERLIN	[GERMANY]
SEPT	24 - 27	2019	ILMAC 2019 | BASEL	[SWITZERLAND]
NOV	5 - 7	2019	BIOPRODUCTION & CPHI | FRANKFURT	[GERMANY]

TRAININGS/WORKSHOPS

NOV	19 - 20	2019	CHROMATOGRAPHY IN PROCESS DEVELOPMENT & PRODUCTION / BASIC COURSE IN ENGLISH | GRIESHEIM	[GERMANY]

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