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Interview

EMA's Senior Medical Officer Hans-Georg Eichler talks about the agency's Adaptive Pathways pilot programme.

Sepsis

The race against time

Exosomes
Nanovesicles take personalised medicine to the next level

Longevity
Endogenous biomarker points to an increased life expectancy

Bioeconomy
Can carbon dioxide emissions act as a feedstock for industry?

CROs & CMOs
Specialists and generalists in the expanding outsourcing market

45% cashback for clinical trials in Adelaide

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COVER STORY

Sepsis: Targeting a silent killer

For over three decades, attempts among drug developers to target the inflammatory pathways and symptoms of sepsis have been fruitless. New rapid diagnostics, rigourous patient stratification and drugs with novel modes of action are now on the horizon for treating the most costly cause of death in the industrialised world. Biotechs are pushing new ideas towards clinical testing, but there just isn't enough funding available in the EU. Will US investors again pick up European innovation on the cheap?

INSIGHT EUROPE

ECONOMY

REGIONAL NEWS

SCIENCE & TECHNOLOGY

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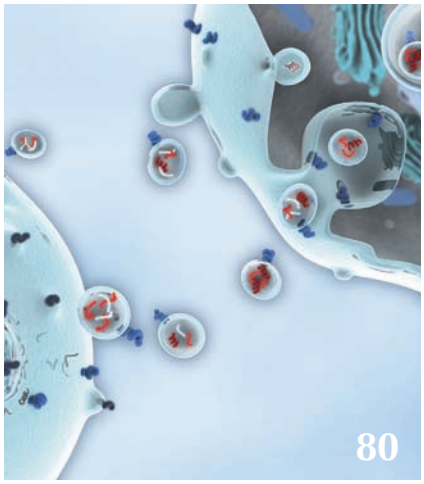
ECONOMY

The CO_2 opportunity

Although most people still view carbon dioxide (CO_2) as a climate killer, industry is beginning to realise that CO_2 could actually provide an abundant, low-cost feedstock for carbon-based processes. A number of Carbon Capture and Utilisation (CCU) schemes are evaluating the many different pathways that could play a role in the field in the future.

BIOSIMILARS



Extracellular vesicles: Better than stem cells?

Disregarded for decades, exosomes are now understood to be a key element in communication between cells. Discoveries around the nano-sized bubbles are revolutionising not only the field of diagnostics. With their ability to mimic stem cells, EVs could also help open the doors to novel therapeutic concepts.

SPECIAL

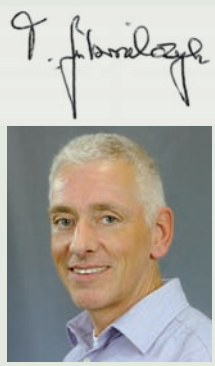
CMOs & CROs

EDITORIAL

What is reality?

Anonymised real-world data that complement data from randomised clinical trails (RCTs) can help companies investigate how their medicines are being used in clinical practice. Boehringer Ingelheim used them in a post-marketing study on patients who receive its blood thinner Pradaxa (dabigatran) antidote Praxbind (idarucizumab). While at the end of August, Takeda started the ever-largest observational study (5,000 patients) to track patterns in disease presentation, patient characteristics, treatment and outcomes in patients with multiple myeloma.

The correlations found are aimed at informing treatment decisions, selecting appropriate patient groups, and evaluating patient benefit. The regulatory consequence of this switch to Big Data collection from medical records, however, may end in a mix of costly RCTs and real-world data in the drug authorisation process (see p. 28). Real-world data could also inform patient stratification in developing new therapies for sepsis, the world's most costly medical complication (see p. 14). And data collected by companies is even helping to establish links between genes, habits and longevity (see p. 86). There's still a major open question, though. Will data-driven correlation sciences – and thus computers – one day be able to describe biological reality, and complement experience-driven medical know-how?



Thomas Gabrielczyk
Editor-in-Chief

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Signal from Australia

BIOSIMILAR SUBSTITUTION In Europe, the Finnish, German, Dutch and Irish Medicines Agencies have clearly taken a stance on the interchangeability of biosimilars under supervision of physicians when well-documented. However, neither a member state agency nor the European Medicines Agency (EMA) itself has ever backed automatic subsitution at the pharmacy level. Although "the theoretical basis for adverse effects is weak", according to Niklas Ekman from the Finnish Medicines Agency (FIMEA), and albeit "clinical crossover studies conducted [so far] have given no evidence of adverse effects due to a switch from a reference product to a biosimilar", Europeans tend to be cautious.

Discussions on the topic at the international level are now set to be revivified by a recent decision of Australia's Pharmaceutical Benefits Advisory Committee (PBAC). In August, one month after the Therapeutic Goods Administation (TGA) granted market authorisation to Samsung Bioepis' biosimilar Brenzys (etanercept), the experts gave pharmacists the authority to substitute the copycat biologic (marketed by Merck & Co) for its reference product, Enbrel (etanercept), marketed by Amgen and Pfizer.

The PBAC said Brenzys "could be marked as equivalent" to Enbrel on the Australian Pharmaceutical Benefits Scheme (PBS), allowing the biosimilar TNF inhibitor's substitution to treat all indications for which both drugs are approved: rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis and non-radiographic axial spondyloarthritis. PBAC noted that a prescriber may choose to not permit substitution of the biosimilar.

The biosimilar was first approved in South Korea while EU authorisation for "Benepali" was given by the EMA this February. ■

Heard in Brussels

In the Brexshit

CLAIRE SKENTELBERY
Secretary General of the European Biotechnology Network

BRUSSELS *Well, those bloody idiots in the UK managed to do it – talk themselves from decades of hysteria about straight bananas (entirely fabricated by one B Johnson during his time as a journalist in Brussels) into actually voting to leave. The UK can now bestride the world once more, free from the shackles of EU tyranny, ready to reassume the economic, social and moral magnificence of its colonial heyday. Look out Zimbabwe, hope you kept all those Rhodesia passports and hey US, they are expecting you back in the same condition in which they left you. Form an orderly queue.*

Imbeciles

Of course this is great for science, as Britain was ACE at that – no need for any kind of plan there. As I was repeatedly told by Brexit campaigners, science and scientific collaboration just happen, they don't need any kind of funding and common framework to help it along. The UK certainly doesn't need any experts, as the whole country was told by the Justice Secretary Michael Gove – so all those pesky Nobel prize winners who said Brexit was a stupid idea can just go back to looking pretty in a lab coat.

Knuckleheads

The UK currently has a strong sector, but for how much longer, given its 1.7% GDP spent on R&D (OECD) is lower than the EU average, bottom of the G7 and far behind Germany's 2.8%? EU funding and collaboration is a vital part of that – especially for UK universities, which dominate EU programmes, and the UK will be walking away from that if freedom of movement is compromised. Once you weaken the innovation base, the industry that grows from it will follow, and it is not just about the money, it is about collaboration and ability to lead international research. The UK will be unable to attract great scientists if their career path is limited, regardless of domestic funding levels.

he impact on UK science has already started. Scientists for EU has recorded more than 40 cases of UK university researchers being asked to leave project consortia for H2020 deadlines after June 23, and we can expect a big drop in UK presence in projects, particularly as coordinators. In big companies, planned posts are being relocated into the wider EU, while scientists from mainland Europe are declining job offers. The EMA will pack its bags in London and take with it the skilled commercial regulatory community that has grown up around it, while the planned EU patent court won't even start. Finally, structural funds to help regions develop better scientific capability are already on hold, even before Article 50 is triggered. Suck it up Wales – you get what you voted for.

National excellence is an international game, especially in science. Being proudly independent/insanely deluded (delete as applicable) comes with a price and the UK does not have the currency to pay the bill. ■

Picture: EBN

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Fooling a silent killer

SEPSIS Although policymakers have grown loud about antibiotic resistance – which currently kills about 80,000 people per year globally – they mostly ignore sepsis, which claims ten times as many lives. Despite a significant lack of funding for clinical validation, a new generation of diagnostics and therapeutics is in the pipeline that promises targeted patient selection and better outcomes within the next five years.

When he was born in 1947, nobody could have predicted that the baby born Cassius Clay would become a three-time boxing world heavyweight champion who would win 56 out of 61 matchups, with 37 knockouts. Last spring, Muhammed Ali – a.k.a. "The Greatest" – lost his final fight. The 74-year-old champion, who suffered from Parkinson's disease in later life, died of septic shock at a hospital in the southwestern US city of Phoenix.

Sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs. It occurs when the body's local response to an invasion and microbial toxins – in Ali's case a respiratory infection – expands to the entire body. The condition is a ruthless, silent killer. Somewhere in the world, someone dies of it around every four seconds. In the nations of the South, collateral damage caused by the systemic infection is greatest. Every year, six million babies and 100,000 mothers from the poorest part of the world die from sepsis, in the throes of symptoms that include uncontrolled inflammation, vascular leakage, severe hypotension, organ damage and shock. It's the most common cause of death by infection there. But even in countries with well-equipped ICUs such as the US, about 260,000 of the 1.1 million patients who are diagnosed with sepsis each year die. With annual costs estimated at US$24bn in 2013 – US$3.4bn more that two years before – sepsis therapy and post-treatment eat up a whopping 7% of the US healthcare budget. In Europe, which counts 1.2 million sepsis infections each year, the situation is no better. Around 40% of all ICU patients die from the amok immune response.

Due to its complex etiology, there is still not a single drug approved for market that could stop the condition's inexorable march. Since the 1980s, drug developers have carried out more than 60 late-stage clinical trails with sepsis drugs that target the molecules triggering host response, but most failed to improve patient outcomes (see graphic p. 16, table p. 18). That's why doctors at ICUs focus on stopping the consequences of sepsis. Standard of care includes:

- surgical removal of the centre of infection
- antimicrobial/antibiotic therapy
- stabilisation of blood pressure, circulation and organ perfusion
- support of organ function.

KONRAD REINHART
Founding President, Global Sepsis Alliance

? What measure is most key in your opinion to prevent deaths from sepsis?

! *Time. Every hour it remains undiagnosed increases the probability it will kill a patient. So the faster you act, the more probable a good outcome. Currently, there is a range of diagnostic biomarkers in clinical development that could trigger a revolution in treatment by accelerating pathogen detection and diagnosis of sepsis and organ failure.*

New tests and biomarkers for early diagnosis

But there is some reason for optimism, according to Konrad Reinhart, the founding president of the Global Sepsis Alliance and author of 800 scientific papers on the subject. He believes that at least a quarter of all sepsis deaths in the industrialised world are preventable if sepsis can only be diagnosed and treated earlier or prevented. "Sepsis is the most common preventable cause of death," he told European Biotechnology. "Every hour sepsis is not diagnosed increases the probability it will kill the patient by 2%. Recognising the early signs of sepsis is therefore crucial. Sepsis is an emergency situation: the faster you act, the better the chance for a good outcome." According to the expert, there are now tests on the horizon that could identify the underlying (mostly bacterial) infection and pathogen within 2-6 hours. Today's gold standard – aerobic and anaerobic blood culture followed by bacterial culture for…

» Read the full story in the printed issue.

Pictures: Dr_Kateryna/fotolia.com (left); Jena University Hospital (right)

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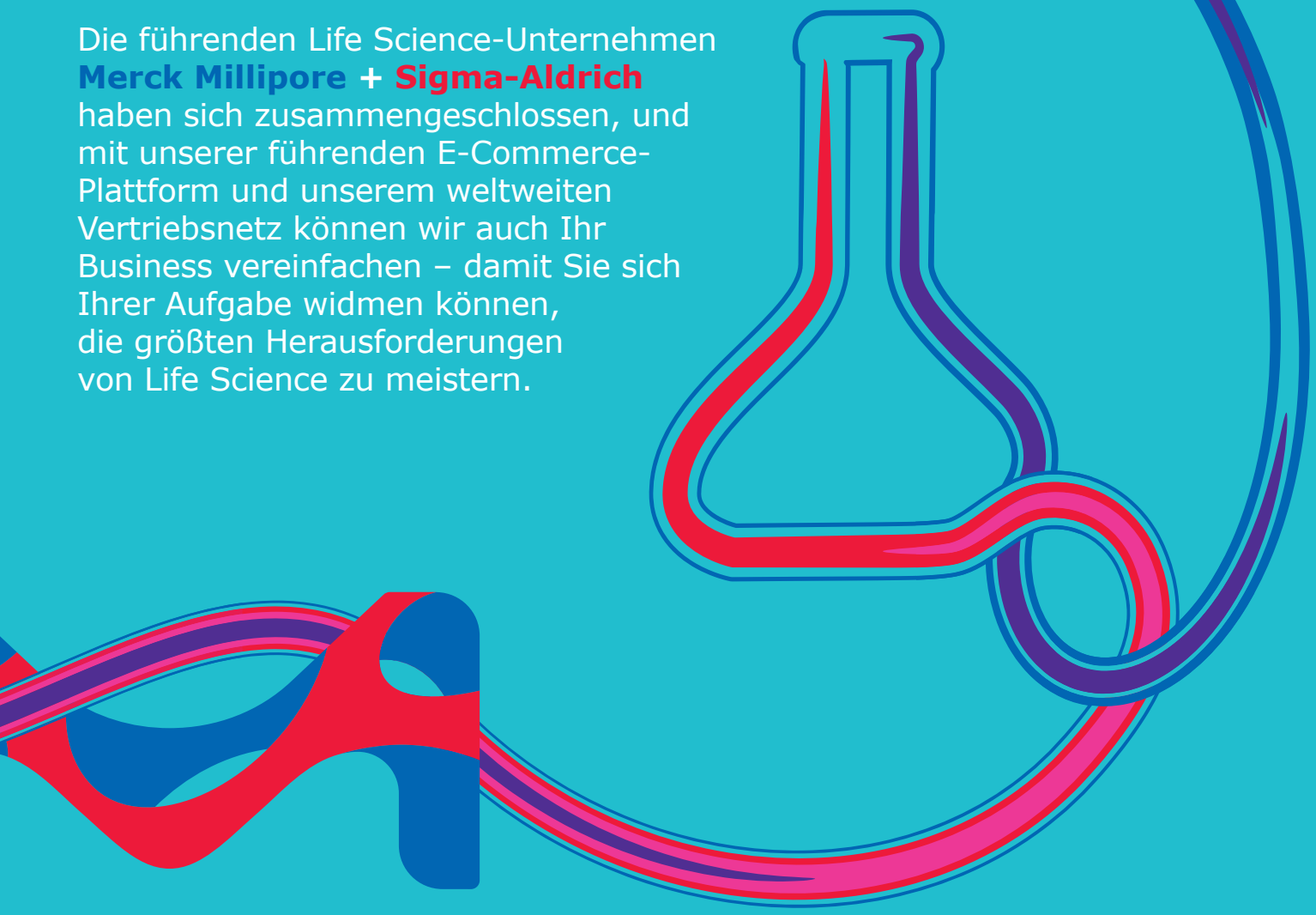

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Climate danger – and opportunity

CARBON CAPTURE AND UTILISATION Perceptions of CO_2 have undergone a remarkable change in the past few years. Although most people still view the gas as a climate killer, Carbon Capture and Storage (CCS) recently began to appear to provide viable options for disposal. Now industry is beginning to realise that CO_2 could provide an abundant, low-cost feedstock for carbon-based processes as well. A number of Carbon Capture and Utilisation (CCU) schemes are evaluating the biological, chemical and physical pathways that could play a role in the field.

›› **Read the full story in the printed issue**.

Picture: Photobank/fotolia.com

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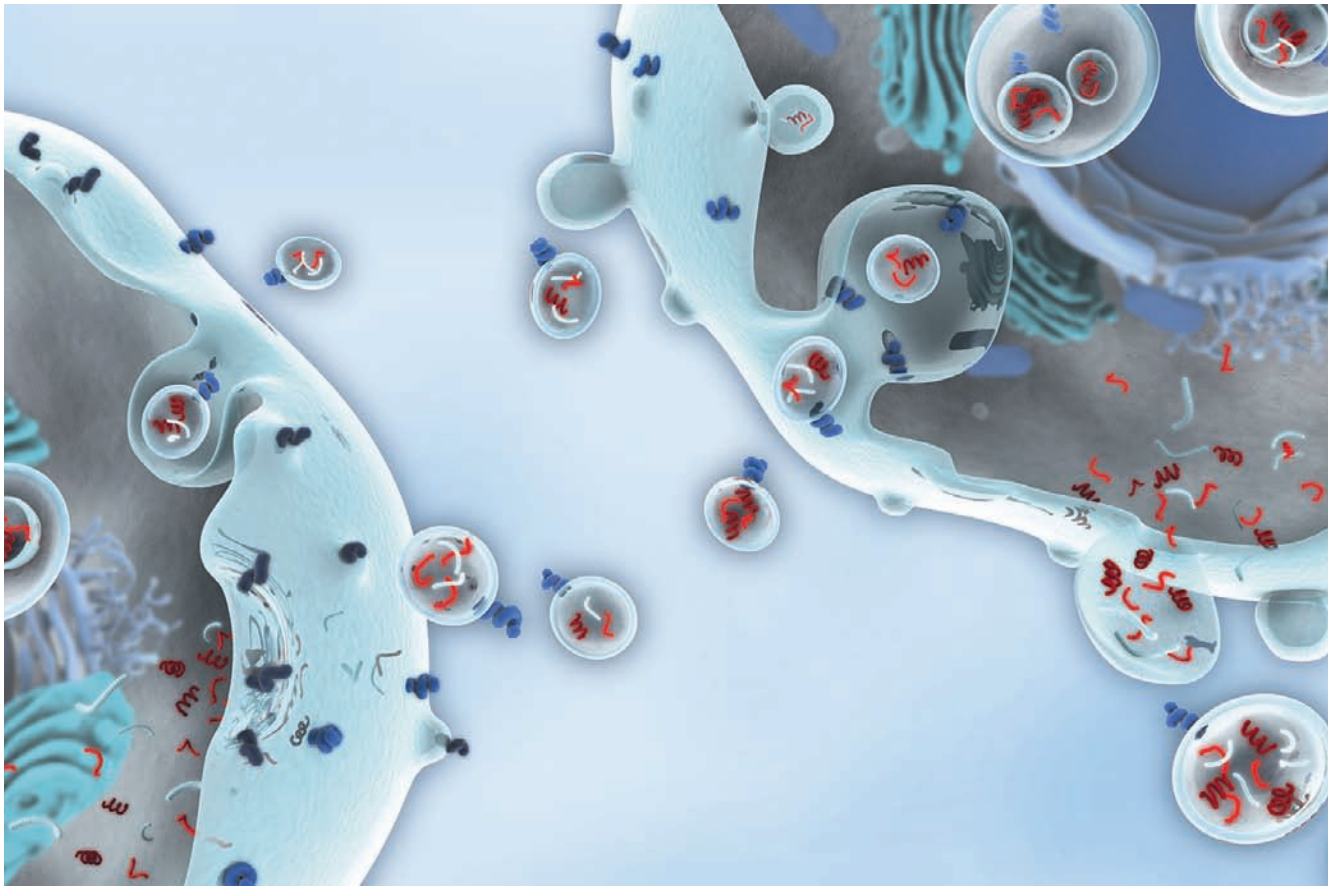

Extracellular – and extraordinary

EXOSOMES Even though they're in the nanometer range, extracellular vesicles (EVs) could start to make it big in the next few years. Long ignored as "cell debris", the tiny bubbles have now been recognized as a key component in the complex communication between cells. EVs carry genetic material and proteins throughout the fluids in the body, and have biological properties comparable to stem cells – but apparently safer. They could serve as vaccines, carry cancer immunotherapies, or play a role in regenerative medicine. Ideas and potential markets are growing fast.

›› **Read the full story in the printed issue**.

Picture: Qiagen

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