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INNOVATORS & IDEAS: ACADEMIC LEADER

Siegfried Kasper: The importance of back-translation of clinical findings to basic science

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Professor Siegfried Kasper, a transformative pioneer in modern psychiatry, serves as Professor Emeritus at the Medical University of Vienna's prestigious Center for Brain Research, where his groundbreaking research continues to revolutionize the understanding of treatment-resistant depression's molecular basis. Following his distinguished tenure as Chair of the Department of General Psychiatry and later Psychiatry and Psychotherapy at the Medical University of Vienna from 1993 to 2019, Professor Kasper has authored over 800 peer-reviewed publications with an exceptional H-index of 131, establishing him as Austria's most frequently cited psychiatrist. His pioneering contributions have focused on demonstrating that psychiatric disorders have a biological basis alongside psychosocial determinants, exploring neuroendocrinological pathways as windows to the brain, and utilizing advanced imaging technologies, including CT, MRT, and PET, to study structural and functional changes in schizophrenia and depression. Professor Kasper was instrumental in introducing revolutionary psychopharmacological treatments, including SSRIs, atypical antipsychotics, and, most recently, intranasal esketamine, demonstrating their effectiveness in specific disease subgroups with improved side effect profiles. As founding president of the Austrian Society of Neuropsychopharmacology and Biological Psychiatry and former President of both the World Federation of Societies of Biological Psychiatry and the International College of Neuropsychopharmacology, he has shaped global psychiatric practice through his leadership of the European Group for the Study of Resistant Depression. His extraordinary achievements have earned him the Grand Decoration of Honor in Silver for Services to the Republic of Austria, the Austrian Cross of Honor for Science and Art First Class, the 2019 City of Vienna Award for Medical Science, the 2024 WFSBP Lifetime Achievement Award, and the 2025 CINP Pioneer Award. In this exclusive Genomic Press Interview, Professor Kasper shares profound insights from his remarkable career dedicated to transforming psychiatric treatment and improving countless lives worldwide.

Part 1: YOUR NAME – Life and Career

Where were you born, and where do you live now?
I was born in Salzburg, Austria, and live right now in Klosterneuburg a suburb of Vienna in Austria.

Could you give us a glimpse into your personal history, emphasizing the pivotal moments that first kindled your passion for science?
As a medical student, I developed a particular interest in brain anatomy. With great enthusiasm, I dissected the limbic system, wondering how emotions and thoughts are transported and modified through this system.

Figure 1. Siegfried Kasper, MD, Professor Emeritus, Medical University of Vienna, Austria.

Please share with us what initially piqued your interest in your preferred area of research or professional focus.
During my specialization, which was at the Central Institute of Mental Health in Manheim Germany, which was in these days, one of the most advanced psychiatric university hospitals in Europe, conducting studies in epidemiology as well as biological mechanisms I was inspired by animal research from Michel Jouvet/France, who noticed that when he lesioned the raphe nuclei in cats they could not sleep anymore. I realized that this is precisely what I do see in my patients: they cannot sleep. Therefore, I started research on the serotonergic system in depression. However, my mentors alerted me that this could be the early ending of my scientific career, since research in depression was in firm hands in those days, with the norepinephrine theory of depression.

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I was fortunate to have one of my first mentors, Helmut Beckman, return from the National Institute of Mental Health (NIMH), and he invited distinguished researchers like Bob Post and Dennis Murphy from the NIMH to visit us in Mannheim. The communications with these colleagues inspired me to join NIMH for further research.

During my research at the Clinical Psychobiology Branch at NIMH, I studied circadian rhythms and the influence of light therapy in seasonal affective disorders (SAD) with Tom Wehr. I conducted the first epidemiological study with Norman Rosenthal on seasonal variations of mood and behavior depending on the latitude the person lived and could demonstrate that further north in the US, higher rates of SAD and its subsyndromal form, a syndrome which I first described, can be found. Japanese colleagues replicated this finding. In addition to changes in mood and behavior, hormonal as well as immunological alterations can be detected with the turn of the seasons.

We would like to know more about your career trajectory leading up to your most relevant leadership role. What defining moments channeled you toward that leadership responsibility?

I was privileged to work in a scientific environment with Heinz Häfner in Mannheim, as well as with Helmut Beckman, who clearly indicated to me that the diseases and, respectively, the symptomatology in our patients have specific mechanisms that await discovery from different angles. In those days, there was an enthusiasm for research in biological mechanisms in Germany, spearheaded also by Hanns Hippius from the Department of Psychiatry in Munich, who visited us several times in Mannheim. He once spoke to me with a confident smile, assuring me that I would have a great future in the field. I still remember these inspiring words very well and continued to use them later in my career when I mentored younger colleagues.

What is a decision or choice that seemed like a mistake at the time but ended up being valuable or transformative for your career or life?

When I started psychiatric training, I thought that psychoanalysis is the way to understand the psyche of our patients better. However, I soon realized that with this approach, I cannot help my patients to get out of the disease, and I was lucky enough to be trained by a psychoanalyst who was a professor of child psychiatry in Heidelberg, who performed genetic studies in so-called "neuroses". He made it clear to me that there are different approaches to understanding the psyche, and psychoanalysis is one way that needs to be connected with profound psychiatric and biological knowledge of the central nervous system. I do not think it was a mistake to perform a complete psychoanalytic training, laying over six years on the couch and exploring my thoughts and emotions, because it showed me how difficult it is to change something in oneself and that we should not ask patients to understand and respectively change something in their life, which we cannot do ourselfs, specifically since this is also not linked to the underlying pathophysiology of their diseases.

What habits and values did you develop during your academic studies or subsequent postdoctoral experiences, that you have maintained throughout your life?

During my academic studies and experience, I needed to listen to the patients carefully, taking into account the existing scientific literature. I also communicated this to my students and younger colleagues. I was often reminded of the saying of Louis Pasteur from 1854, "In the field of observation, chance favours only the prepared mind". With this in mind, the development of new underlying mechanisms for the better understanding of the patient can be developed in a back-translational manner.

Please tell us more about your most relevant focal points – past or present – within your chosen field of science.

Earlier studies dealt with the effect of light therapy in seasonal affective disorder (SAD), and interestingly, a patient once correctly informed me that this disease should be called light deficiency disorder instead of seasonal affective disorder (SAD). This inspired me to conduct a study in São Paulo, Brazil, in which we could demonstrate that higher rates of depression emerged during the rainy monsoon season, coinciding with light deficiency in the working population. During my time at the psychiatric department at the University of Bonn in Germany with my longtime good friend Hans-Jürgen Möller as chair, we had a close collaboration with neurologists as well as neurosurgeons. A colleague from the Department of Epileptology once informed me that patients are quite happy after undergoing transcranial magnetic stimulation (TMS) to identify an epileptogenic focus, which helps guide neurosurgeons during planned operations. I asked my colleague if side effects accompany this method, and after he assured me that this is not the case, he performed this TMS methodology on me. He set the coil on my right hemisphere, and I realized that the left thumb was moving without my will. I did not have any changes in my mood, since I was also not depressed, and there were no side effects.

Thereafter, we introduced this methodology first to depressed patients and witnessed an antidepressant response. However, publishing these results was quite challenging, but we managed to do so. I was pleased to see that TMS developed excellently, and it is often overlooked that our roots in psychiatry are in my group in Bonn, Germany. Together with my team at the Medical University in Vienna, we conducted a large number of neuropsychopharmacological studies, and nearly all medications currently on the market were studied in our group, mostly within multicenter trials, demonstrating efficacy and fewer side effects compared to the older compounds. In schizophrenia, an additional benefit for depressive and so-called negative symptoms could be demonstrated.

More recently, I have been focusing on treatment-resistant depression (TRD) and working with a European group on this topic (GSRD: group for studies of resistant depression). We sampled over 3000 patients in different European countries and recorded clinical as well as biological variables. We could show that symptoms like severity, anxiety, and suicidality within depression, as well as the number of previous episodes, are linked to TRD. We performed whole genome analysis, and it looks like the structures that we are usually interested in, the monoamine transporters or serotonin receptors, do not show any genetically differentiating pattern in patients who respond or do not respond to antidepressant treatment. Based on our studies, we also defined treatment-resistant depression, not responding to two antidepressant trials, irrespective of mechanisms of action, given in sufficient length and dosage, as TRD patients. We were pleased that the European health regulatory authorities (the EMA) also adopted this definition. Several studies, including those for the development of intranasal esketamine, utilized our definition and subsequently brought this medication to market.

What were the key impact areas of your research topics?

The key impact areas of my research were always patient-centered. Early studies covered topics on psychopathology, such as catatonia. I could show that patients with malignant catatonia are not treated anymore by psychiatrists but in internal medicine and therefore are not vanished. A large number of studies have been carried out in neuropsychopharmacology, such as the introduction of the serotonin-reuptake inhibitors (SSRIs) as well as atypical antipsychotics for schizophrenia. A part of my research was also related to phytopharmacology. I insisted to the groups I worked with that phytopharmacological compounds should be studied in the same manner as chemical substances, and based on this approach, St. John's Wort, as well as Silexan, a standardized Lavandula extract, exhibited positive results in randomized controlled trials for depression and anxiety disorders, respectively.

What have you most enjoyed in your capacity as an academic or research leader?

I thoroughly enjoyed the discussions and collaborations with bright, often young colleagues who questioned what was so clear to me. I was enthusiastic to see how rigorously they performed studies under my guidance. I also enjoyed organizing national and international congresses in Vienna and abroad. I founded the Austrian Association for Neuropsychopharmacology and Biological Psychiatry (ÖGPB), and I was the president of the World Federation of Societies of Biological Psychiatry as well as the president of the Collegium Internationale Neuropsychopharmacolorum (CINP), both of which represent a worldwide research community for advancement of the knowledge in the field.

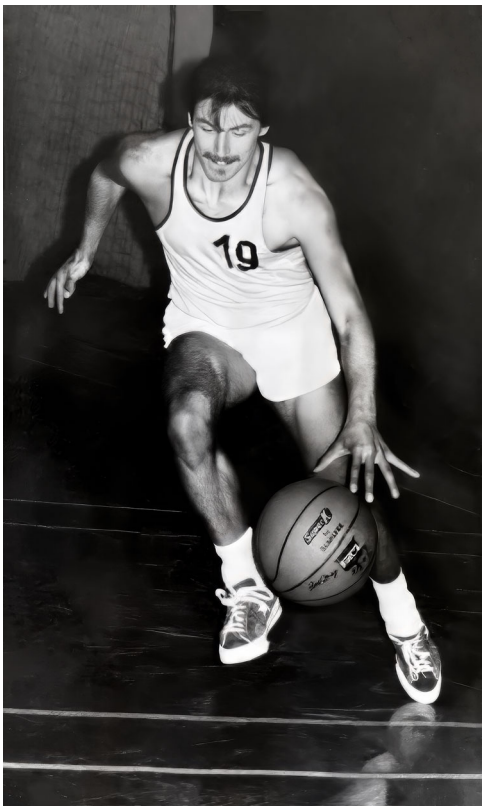

Figure 2. Siegfried Kasper in his youth as a point guard for an Austrian second division basketball team, wearing jersey #19. Despite being the smallest player on the team, his athletic background would later inform his understanding of psychological barriers to learning, as he observed while teaching skiing.

At Genomic Press, we prioritize fostering research endeavors based solely on their inherent merit, uninfluenced by geography or the researchers' personal or demographic traits. Are there particular cultural facets within the scientific community that warrant transformative scrutiny, or is there a cause within science that you feel strongly devoted to?
Most of my research has been carried out in Germany and Austria; however, during my stay at the National Institute of Mental Health, I also performed studies on US citizens. I was aware that cultural facets need to be considered when interpreting study results. For instance, I performed a study with a Japanese colleague comparing paranoid delusions in Japanese and German patients and realized how different the contents were; however, the structure of the delusions was identical.

Outside professional confines, how do you prefer to allocate your leisure moments, or conversely, in what manner would you envision spending these moments given a choice?
I love nature, and I work with great pleasure in my garden and at my informal scientific outpost in southern Italy, specifically in Puglia, where I enjoy olive trees and maintain my small vineyard with primitivo grapes. Furthermore, I am thrilled to have a wonderful dog around me, always the same race. This Lakeland terrier brings me much joy through communication, and she reminds me that there are biological rhythms for activities like playing and walking. I have slowed down quite a bit with sports. However, when I was young, I was a basketball player in the Austrian second-highest league (see Figure 2). As the smallest player on the team, I mostly played point guard. Coming from Austria, of course, skiing was high on my mind. I was a ski instructor, and as a ski instructor, I probably did my first psychiatric interventions, because I could see very fast if a person was able to learn skiing or not, like having anxiety was always a negative predictor for learning to ski.

Part 2: YOUR NAME – Selected questions from the Proust Questionnaire[1]

What is your most marked characteristic?
I am impatient and always looking for new things. If I discovered something, I would lose interest and want to move on. Furthermore, I am stubborn and very determined. I never give up. When I have an idea, I want it to come to life.

Among your talents, which one(s) give(s) you a competitive edge?
Among my talents, the competitive edge is that I am always interested in new ideas, and if I reach a goal, I do not sleep on this pillow, but I am ready to embark on a new area.

If you could change one thing about yourself, what would it be?
I would change my impatience.

What is your current state of mind?
I think I am fine. I love to live and hope that this will go on for quite a while, since I am already approaching the age of 75, luckily without a severe disease.

What is your idea of perfect happiness?
Perfect happiness is like Sigmund Freud pointed out, the ability to work and love, and if you combine both of these things with the right persons and cultural environments, then the likelihood of having perfect happiness is very high.

When and where were you happiest? And why were so happy then?
I am always happy when I reach a goal, like when the NIMH invited me to be a fellow or when the scientific community voted for me as president of the World Federation of Societies of Biological Psychiatry. I was so happy because this indicated to me that I could proceed with another step in my life.

What is your greatest fear?
My greatest fear is having a severe illness that disables me.

What is your greatest regret?
My greatest regret is that I did not spend enough time with my loved ones.

What are you most proud of?
I am most proud of my academic achievements, which I share with my colleagues, and am always thrilled to meet again.

What do you consider your greatest achievement?
My most outstanding achievement was conducting studies that transformed the treatment and understanding of our patients.

[1]In the late nineteenth century, various questionnaires were a popular diversion designed to discover new things about old friends. What is now known as the 35-question Proust Questionnaire became famous after Marcel Proust's answers to these questions were found and published posthumously. Proust answered the questions twice, at ages 14 and 20. In 2003 Proust's handwritten answers were auctioned off for $130,000. Multiple other historical and contemporary figures have answered the Proust Questionnaire, including among others Karl Marx, Oscar Wilde, Arthur Conan Doyle, Fernando Pessoa, Stéphane Mallarmé, Paul Cézanne, Vladimir Nabokov, Kazuo Ishiguro, Catherine Deneuve, Sophia Loren, Gina Lollobrigida, Gloria Steinem, Pelé, Valentino, Yoko Ono, Elton John, Martin Scorsese, Pedro Almodóvar, Richard Branson, Jimmy Carter, David Chang, Spike Lee, Hugh Jackman, and Zendaya. The Proust Questionnaire is often used to interview celebrities: the idea is that by answering these questions, an individual will reveal his or her true nature. We have condensed the Proust Questionnaire by reducing the number of questions and slightly rewording some. These curated questions provide insights into the individual's inner world, ranging from notions of happiness and fear to aspirations and inspirations.

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Figure 3. Professor Siegfried Kasper (right) with colleague Hans-Jürgen Möller, former Chair of Psychiatry at Ludwig-Maximilians-University Munich and past President of the Collegium Internationale Neuro-Psychopharmacologicum (CINP), standing beside the bust of Emil Kraepelin, the pioneering psychiatrist who transformed psychiatry into a scientific discipline. Kasper considers Kraepelin one of his greatest inspirations, noting he "would love to have dinner with Emil Kraepelin because he shaped Psychiatry into a scientific discipline and he was already traveling all over the world."

What or who is your greatest passion?
My greatest passion is conducting research and helping to uncover mechanisms that improve the lives of psychiatric patients.

What is your favorite occupation (or activity)?
My favorite occupation is writing articles on psychiatric topics. Additionally, I enjoy giving lectures and traveling to different countries, where I hope to understand our common problems through discussions with colleagues.

What is your greatest extravagance?
My greatest extravagance is that I like to have new cars, which should be well-equipped with technical toys.

What is your most treasured possession?
My most treasured possession is likely our house, which I share with my wife, Anita, in the neighbourhood of Vienna, and another one in Puglia, southern Italy, which I affectionately call my scientific outpost. It is nestled in an olive grove. Furthermore, I am delighted to have old textbooks, and probably the most treasured book is "The Antomy of Melancholy" by Robert Burton, published in 1651. I was lucky to buy this book during a meeting in Chicago when I was a young doctor, which nearly ruined my financial budget.

Where would you most like to live?
I like where I am living right now. This is a perfect place.

What is the quality you most admire in people?
I admire people who are open, honest, and happy, and who are sometimes ready for a joke.

What is the trait you most dislike in people?
What I dislike most in people is dishonesty and playing dirty games, especially when they fail to uphold an agreement we have reached.

What do you consider the most overrated virtue?
The most overrated virtue is being spendable.

What do you most value in your friends?
I value my friends most when they are open and I can count on them.

Which living person do you most admire?
A schizophrenic patient of mine who arranged to live with the burden of his disease.

Who are your heroes in real life?
I greatly value Viktor Frankl, whom I was fortunate to meet in person while he was still alive.

If you could have dinner with any historical figure, who would it be and why?
I would love to have dinner with Emil Kraepelin because he shaped Psychiatry into a scientific discipline, and he was already traveling all over the world, including Indonesia (see Figure 3).

Who are your favorite writers?
Milan Kundera, Thomas Bernhard, Ernest Hemingway, and Erich Fried.

Who are your heroes of fiction?
I do not like fiction; I never read fiction.

What aphorism or motto best encapsulates your life philosophy?
Stay tuned and be the pilot of your life.

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