Molecular Microbiology (2013) 88(2), 219–221 ■ doi:10.1111/mmi.12198

Obituary

Alexander Böhm (1971–2012)

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Summary

On November 28, 2012 Alexander (Alex) Böhm, a bacterial geneticist, died at age 41, only a few months after taking up a position as an assistant professor at the LOEWE Center for Synthetic Microbiology in Marburg, Germany. Earlier in 2012 Alex had been diagnosed with an aggressive form of thyroid cancer that left him little time to live his scientific and personal dreams.

Alex Böhm studied biology at the University of Konstanz, Germany. Already in the introductory Microbiology course given by his long-term teacher and mentor Winfried Boos, Alex became interested in complex signal transduction pathways, in particular bacterial chemotaxis. Motivated by his mentor's long-standing connection to galactose chemotaxis via the first "chemoreceptor", the galactose binding protein, Alex wanted to delve deeper into the bacterial chemotaxis world. Accordingly, Sandy Parkinson agreed to host him in Salt Lake City for his diploma thesis.

Alex spent much of 1996 in the Parkinson lab, investigating the elusive molecular mechanism of chemotactic responses to substrates of the PEP-dependent carbohydrate phosphotransferase system (PTS). To test the idea that PTS inputs converged on the chemotactic signaling kinase, CheA, Alex isolated many hundreds of CheA mutants, hoping to find one that was defective in chemotaxis toward PTS substrates, but not toward compounds detected by conventional chemoreceptors, the so-called "methyl-accepting chemotaxis proteins" (MCPs). Alex never found such a mutant, but he did become a card-carrying bacterial geneticist in the process. Here's an excerpt from one of Alex's progress reports on his project: "None of the mutants uncouples PTS-dependent from MCP-dependent chemotaxis! However, a large collection of independent mutants piles up in the freezer and wants to be characterized!" Note that Alex used exclamation points in his reports, usually to show his delight in unexpected, or even unwanted, experimental results. Also note that Alex not only appreciated mutants, but knew, with a geneticist's instincts, that mutants WANT to be characterized, for only then will their secrets come to light.

In 1997 Alex returned to Konstanz for his Ph.D. and quite naturally took up the "Chemotaxis" lecture in the Microbiology course. Ever since then chemotaxis has been an integral part of the Kompaktkurs in Konstanz. Still today the frame of Alex' excellent presentation is being used for teaching. In Konstanz Alex became part of the maltose crew. In no time had he learned the ABC of maltose transport and began to cooperate with the King (Howard Shuman in New York) and the Queen (Evelyne Richet in Paris) of the maltose kingdom. Alex became fascinated by the involvement of the MalK protein, the ATP-hydrolyzing subunit of the transporter in the regulation of *mal* gene expression. It was known that null mutants in MalK were constitutive for *mal* gene expres-

sion, whereas overexpression of MalK repressed expression. MalK interacted with and inactivated MalT, the transcriptional activator of all *mal* genes. Alex genetically defined the surface of MalK that interacts with MalT and located his mutations to the "regulatory subunit" of MalK, which as a truncated peptide was as effective in MalT inhibition as intact MalK. How did it work? Was there a MalK cycle in which idle MalK in the absence of transport would dissociate from the transport complex and inactivate MalT? Alternatively, was there a MalT cycle where MalK would never dissociate from the transport complex, but bind and inactivate MalT in the absence of transport, then release it during transport, allowing it to become a transcriptional activator? Through a number of elegant experiments Alex was able to exclude the MalK cycle but, at that time, was unable to provide strong evidence for the MalT cycle (Böhm *et al*., 2002). This was finally achieved and published in 2012 in Molecular Microbiology by Richet and coworkers, long after Alex had left the maltose scene.

Alex was a wandering encyclopedia for many things. For example, as a football aficionado he had an astonishing recollection of details regarding scores, players and games dating years or even decades back. This made him a true expert in reading and interpreting the game. Similarly, he had profound insight and detailed understanding of *E. coli* physiology, remembering every little detail that had been published. This, in turn, made him a true authority in understanding *E. coli*. His other "love" in Science was Genetics, a discipline, which he was well trained for during the years he spent with Sandy Parkinson and Winfried Boos and which he had chosen as a means to dissect some of *E. coli*'s regulatory complexity. Like many other young microbial scientists in the past decades, Alex received his "inauguration" into Bacterial Genetics when attending the Advanced Bacterial Genetics summer course in Cold Spring Harbor in 1998 (instructors: Bonnie Bassler, Colin Manoil and Jim Slauch). In his Ph.D. work in Konstanz and more so later, after he had left the city, Alex was wrapped up in fancy regulatory mechanisms of bacterial gene expression and cell behavior. His mind was always wide open for the unexpected. In his opening statement of his Ph.D. thesis submitted in 2002, he cites Jon Beckwith and Tom Silhavy in *The Power of Bacterial Genetics*: "Perhaps the most important principle to emerge out of the study of gene expression is that general principles do not exist".

In 2005 Alex joined the lab of Urs Jenal at the Biozentrum of the University of Basel as a postdoc. He joined with a rucksack full of enthusiasm, wonderful ideas and his love for *E. coli*, which he had planned to combine with some of the ongoing research in the lab on c-di-GMP signaling. At this time microbiologists became aware of the importance of c-di-GMP for bacterial growth and behavior and of its profound influence on some basic life-style decisions that bacteria need to make in order to compete and survive. Alex quickly realized that studying the c-di-GMP signaling network in *E. coli*, based on its anticipated complexity and behavioral importance, would be a very fruitful and rewarding endeavor. Alex was interested in how c-di-GMP controls *E. coli* behavior through its inhibitory and stimulatory effects on motility and surface-based growth, respectively. He decided to study the processes and mechanisms by which c-di-GMP licenses motility and biofilm formation in this organism. Following up on some earlier observations by Chankyu Park at the KAIST in Korea who had identified several components of the c-di-GMP network regulating *E. coli* motility (Ko and Park, 2000), Alex dissected the pathway by which c-di-GMP modulates flagellar motor function. He showed that YcgR, a small c-di-GMP binding protein with a PilZ domain, in its ligand-bound form, localizes to the flagellar motor where it interacts with the stator complex to slow down flagellar rotation like a molecular brake, thereby adjusting swimming velocity in response to changing environments (Böhm *et al*., 2010).

In parallel, he began to explore the 'other side of the coin' and started investigating *E. coli* biofilm formation. Screening through a chemical library he discovered that subinhibitory concentrations of translation inhibitors strongly stimulated biofilm formation through the production of the exo-polysaccharide adhesin poly-GlcNAc. These studies concluded that two small signaling molecules, c-di-GMP and ppGpp, were required to activate the poly-GlcNAc synthesis machinery, also called PGA, in response to translation interference (Böhm *et al*., 2009). While the exact role of ppGpp in this regulatory step is still elusive, Alex, together with Samuel Steiner, went on to dissect how c-di-GMP activates PGA. At the focus of these studies were PgaC and PgaD, two PGA components located in the inner membrane of *E. coli*. As an annotated glycosyltransferases (GT), PgaC appeared responsible for sugar polymerization and seemed an obvious target for the allosteric action of c-di-GMP. PgaD, in turn, popped up in Alex' studies as a small accessory membrane protein, the stability of which strictly depended on the availability of c-di-GMP. In a wonderful piece of work Alex and Samuel used genetics and biochemistry to demonstrate that c-di-GMP binds to both PgaC and PgaD, thereby mediating their direct interaction in the membrane and stimulating their GT activity (Steiner *et al*, 2012). These studies, initiated by Alex years before, made PGA the first c-di-GMP regulated EPS machinery in bacteria for which some of the details of c-di-GMP mediated allosteric control were uncovered.

After his years in Basel, Alex joined the Institute for Molecular Infection Biology (IMIB) in Würzburg as an independent group leader in October 2010. IMIB was familiar to him through his collaboration with Ulrich

Dobrindt on uropathogenic *E. coli*. Nonetheless, Alex joined at a very exciting time when IMIB had just moved to a new building, appointed a new director and recruited several young group leaders. He set up shop, successfully applied for his first grants and hired his first PhD students. Formally speaking, he was not senior to the other young investigators at IMIB, though his experience, both personal and scientific, as well as his reassuring self-confidence and positive attitude soon made him the leader of the pack. He quickly made friends with the groups of Daniel Lopez and Cynthia Sharma and many members of the Vogel lab with whom he initially shared lab space and equipment. While at IMIB, Alex was a walking encyclopedia of bacterial gene functions and a never-dwindling source of advice regarding the proper set up of a genetic screen. Moreover, his passion for teaching made him extremely popular with students.

Scientifically, he kept pursuing c-di-GMP, but instead of using *E. coli* K12 he now began to investigate its role in uropathogenic *E. coli* strains. This made him run his first RNA-seq experiments, to discover both promoters and small RNAs that responded to depletion or overproduction of c-di-GMP. In addition, he was keen to understand biofilm-breaking substances that were identified through a screen he had designed in Basel. Finishing other previous projects kept him busy, too; for example, in collaboration with Tilman Schirmer, an X-ray crystallographer from the Biozentrum in Basel, he discovered a crucial role for zinc ions in c-di-GMP homeostasis.

One event of that time Alex will always be remembered for is the Würzburg Mol Micro Meeting, which IMIB began to organize together with *Molecular Microbiology* in 2011. This meeting aimed at fostering the field that is represented by this journal's publications, which is also the home turf of most IMIB researchers. Alex did an outstanding job as the lead organizer for the first meeting (Böhm *et al*., 2011), helping to identify the publications that formed that basis of the invited speaker list, helping speakers plan their trip to Würzburg, and making sure things would go smoothly during their stay here. Much of the success of this first and the subsequent 2012 meeting owes to his tireless commitment.

While he was building his group in Würzburg, his third child was born in September 2011 and in February 2012 Alex decided to accept an offer from the LOEWE Center for Synthetic Microbiology in Marburg for an assistant professorship. Here Alex planned to continue his work on biofilm formation and c-di-GMP signaling, but in addition he set out to construct synthetic biofilms using light-controlled synthetic signaling pathways. To lure Alex away from Würzburg, the Center for Synthetic Microbiology and the Max Planck Institute for Terrestrial Microbiology had joined forces to create an attractive offer that would give Alex and his family a long-term perspective. When the news broke that Alex had accepted the position, the enthusiasm was immense in the entire microbiology community in Marburg. Alex and his family moved to Marburg in the summer of 2012 and with his endless enthusiasm, excitement, curiosity, knowledge and helpfulness he immediately became someone that everybody sought out for advice. In fact, "we should talk to Alex about this" became a regular phrase in Alex's few months in Marburg.

Alex was a wonderful teacher and scientist; creative, inspired and inspirational. He got people excited. He liked to make models and play with ideas. He liked to know and learn about the projects going on around him. He liked to make suggestions not always to the fancy of the recipient. And, yes, he was impatient. Where there was a shortcut, Alex would find it. Herman Kalckar, the research adviser of one of the authors (W.B.) from the old days in Boston, used to divide scientists into two categories: Dionysians and Apollonians. A Dionysian would get the solution to the problem in a dream with experiments only being a painful and unfortunate necessity. In contrast, an Apollonian would insist on repeated experimental evidence and with his mind being blocked by rules and regulations, new ideas would not be his asset. Alex always set great store by solid experimentation. Nevertheless, we believe that with Alex we lost a Dionysian. But many of us lost more than a highly gifted and creative scientist. We lost a very good colleague and friend.

Alex Böhm is survived by his wife Vera and by his three daughters Hanna, Julie, and Emmy.

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