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in combination with other polymers, were presented as the first replicating genomes of living cells on earth.

Sid visited Israel several times. Once he told me that he spent a few months working in exhausting farming in a moshav, Nahlal, before pursuing his academic studies in the United States. Later, as an independent principal investigator at Yale, he had ties with the Weizmann Institute of Science and collaboration with his close friend

Raymond Kaempfer. In 2013, Sid received an honorary doctorate from the Hebrew University of Jerusalem. In this several millennia old city, he liked its unique cuisines and enjoyed its cold weather at night. The last time I met Sid was in the King David Hotel of Jerusalem in 2019 before the start of the coronavirus pandemic. He advised me that a person should take care of himself and enjoy life.

## IN MEMORY OF PROFESSOR SIDNEY ALTMAN: INSPIRING PEOPLE TO THE FULL

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Photos of Sid with the authors. (Left) Sid and Ge during a press interview in the lab at Yale University in 2003. (Middle) Sid and Taijiao during Sid's visit to Beijing in 2006. (Right) Sid and Li during a lab reunion in the Department of Molecular Cellular and Developmental Biology at Yale University in 2015. (Photo courtesy of Ge [left], Taijiao [middle], and Li [right].)

Sidney (Sid) Altman is recognized globally for the discovery of an RNA catalyst in RNase P. For the three of us, however, our time with him showcased his influential role as an inspiring mentor. Here, we reflect on our training with Sid, which encouraged us to pursue different career paths after leaving his laboratory.

All three of us graduated from the Shanghai Institute of Biochemistry and Cell Biology (SIBCB), Chinese Academy of Sciences (CAS). SIBCB is prominent for its contributions to biochemistry, molecular biology and cell biology having made an early mark through the synthesis of crystalline bovine insulin in 1960s. Trained as graduate students in three different SIBCB labs, all three of us had strong experience in RNA molecular biology, and importantly, were fascinated by the complexity and diversity of RNA. Luckily, we got an opportunity to work with Sid as postdoctoral fellows (Taijiao 1999–2002; Ge 2003–2004; Li 2004–2006), focusing on different aspects pertaining to the characterization of RNase P and use of this enzyme as a tool to regulate gene expression by the external

guide sequence (EGS) technology. Although we had been involved in different projects there, we had all done the same very first experiment at Sid's laboratory: Test the catalytic activity of *Escherichia coli* RNase P RNA subunit!

While our research objectives were different, we had an overarching sentiment of Sid's complete devotion to research and striving for the best. Such an assessment was shaped by his open-door policy for discussion when we encountered unexpected results or needed help to solve problems. Sid's own enthusiasm for the work was evident by the fact that he would come to our lab benches regularly to learn of our results first-hand (see photo, left). Hard copies of our manuscript drafts were edited carefully. He made sure that we wrote concisely without compromising the main message and ensured that redundancies were eliminated. These exchanges were formative especially for non-native English speakers.

Transitioning from graduate students to postdocs is never easy, a difficulty heightened when one crosses borders

to a new country with different norms. However, our research and lives were fruitful and joyful because Sid and all lab members were supportive and ensured our professional and personal well-being. Sid liked to have a cup of coffee during morning breaks. Quite often, Sid also joined us during lunch time to share with us some scientific and non-scientific developments he thought interesting. Sometimes, Sid gave us a ride across New Haven, and he would narrate stories associated with some historical buildings at Yale. While we were so happy to learn about the past, we could also appreciate his pride of Yale, where he had worked during his entire independent career.

Around the time we joined Sid's laboratory, life science research was continuously booming largely due to the advent of new technologies, the completion of the human genome project, and the subsequent observation of genome-wide expression of noncoding sequences. Accordingly, we had opportunities to explore different research directions with the guidance of Sid at his laboratory and obtained his full support when choosing different career paths. After leaving his laboratory, we maintained ties with Sid and found opportunities to meet him in person. For example, Taijiao showed Sid around in Beijing when he was invited to China for academic activities (see *photo, middle*) and

Li went to Yale for the lab reunion to share research in progress with Sid and many other lab alumni (see *photo, right*). During our conversations, Sid's sharp intellect was always evident. He would convey crisp thoughts on projects that we were focusing on, and importantly, gave positive feedback on our achievements. This encouragement, which sparkled in his eyes, inspired us to move forward. After learning that we worked very hard with little time to spend with our children, he shared his joy when he spent time with his children and grandchildren and suggested to us to schedule more time with our families. Such counsel strengthened our personal ties to him.

In recent times, despite his illness, Sid was still optimistic and even talked about travel to China. Due to the COVID19 pandemic, we had no chance to meet Sid in person after the lab reunion in the summer of 2019. In early April 2022, even while we were locked down due to the outbreak of omicron in different cities in China, we were saddened to learn of Sid's demise. At such difficult times, we all take recourse by reliving our cherished memories. Sid's integrity and dedication to science and mentoring remain useful beacons for us. While we deeply miss his enduring support and inspiration, we recognize that we were extremely fortunate to have worked with him.

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## HALF A CENTURY WITH SIDNEY ALTMAN

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I met Sidney Altman soon after he came to Yale from the MRC Laboratory of Molecular Biology, Cambridge, UK, where he initiated with John Smith and Sydney Brenner studies on tRNA precursors in prokaryotes. When he first came to Yale, I went up to the 8th floor of the Kline Biology Tower and saw a person walking down the hall that I presumed was Altman and, knowing that he was originally from Montreal (near where I grew up), I hollered a greeting in French Canadian. I was in turn greeted by a long reply in perfect French-Canadian dialect, the nature of which I will not repeat here. This exchange was the beginning of our 50-year friendship.

Initially, I must say that I was not particularly interested in Sid's project on tRNAs and the RNases that might be processing them, until his papers in the late 70s showed that there was a definite RNA moiety involved in the enzymatic processing of the tRNA. This information came to me through Sid's graduate student, Ben Stark, who was friendly with students in my own laboratory (see Ben Stark's contribution in this tribute) and Peter Rae, a new Assistant

Professor who had joined us from the University of Chicago. Ben's PhD project was to purify bacterial RNase P, and during one of his meetings with his thesis committee, in which Rae was a member, Ben related his difficulties in the enzyme purification because of what seemed to be an "anionic contaminant." Rae suggested that Ben treat the crude enzyme preparation with a nonspecific ribonuclease in case the "contaminant" was RNA and offered a suggestion to also inactivate it given the subsequent need to assay RNase P. In hindsight, this suggestion seemed reasonable, but I suspect, at the time, the idea of treating a crude preparation of RNase P with ribonuclease probably engendered some chuckles. The rest is history, of course, as this experiment established the requirement of an RNA for RNase P activity.

As the papers of Sid Altman and his colleagues began to be published on the RNA moiety of RNase P, he had a hard time convincing his colleagues, not only those working on RNA at Yale, but internationally, that he had an RNA essential for enzymatic activity on a tRNA