

# Prof. Arno F. Spatola's founding role at Peptides International

Peptides International, located in Louisville, Kentucky (USA), was founded by Prof. Arno F. Spatola, PhD, in 1983 as a biochemical company specializing in peptide-related products. The company is now celebrating its 20th anniversary. Dr Spatola was President and Chief Executive Officer of Peptides International until his sudden and unexpected death in July of 2003.

Arno F. Spatola was born in Albany, New York, in 1944. He received his undergraduate degree in chemistry with a minor in political science from Cornell University and his Master and Doctorate degrees from the University of Michigan with mentor, Prof. Daniel T. Longone. Under the direction of Dr Victor J. Hruby at the University of Arizona, Arno's postdoctoral research focused on peptide synthesis and structure–function studies, marking the beginning of his distinguished career in peptide science. This led to his 1973 recruitment by the University of Louisville's (U of L) Chemistry Department to initiate a peptide research program in Louisville, Kentucky.

While at U of L, Prof. Spatola became an internationally recognized chemistry researcher. During his remarkable career, his major research interests included biologically active peptides, pseudopeptides, cyclic peptides, and cyclic peptide libraries. He originated the 'Ψ (psi) bracket' pseudopeptide nomenclature, formally adopted by IUPAC. Notable contributions include Dr Spatola's development of backbone-modified peptides (including  $\psi[\text{CH}_2\text{S}]$ ,  $\psi[\text{CH}_2\text{SO}]$ ,  $\psi[\text{CH}_2\text{NH}]$ , and  $\psi[\text{CSNH}]$ ), matrix metalloprotease (MMP) inhibitors, ammonium formate catalytic transfer hydrogenation (AFCTH), and cyclic peptide libraries.

Dr Spatola taught organic and combinatorial chemistry and directed the research of numerous graduate and undergraduate students. He was also a member of the Department of Biochemistry and Molecular Biology and

collaborated with many research groups involved in biomedical investigations. Spatola authored over 140 papers including six patents for his research. In 1982 and in 1990, under Dr Claudio Toniolo, Dr Spatola served as a visiting professor at the University of Padova, Italy.

In 1996, Spatola founded and served as Executive Director of the University of Louisville's Institute for Molecular Diversity and Drug Design (IMD<sup>3</sup>). IMD<sup>3</sup> is a multidisciplinary research and training program focussing on drug design and discovery. Its goal is to discover new cures for major diseases while exposing students to the teamwork essential to solving most modern research problems. Since 1999, IMD<sup>3</sup> has offered a yearly symposium on drug discovery that attracts nationally and internationally acclaimed speakers and participants.

During the first-ever curriculum course of its kind in combinatorial chemistry, Arno hosted notable speakers, such as Mario Geysen (University of Virginia) and Richard Houghten (Torrey Pines Institute) at U of L. In 2000, H. Mario Geysen and Ralph F. Hirschmann (University of Pennsylvania) were among the invited speakers at IMD<sup>3</sup>'s first annual symposium held at Jewish Hospital in Louisville, the eventual site of the world's first implantable replacement heart. Arno, a kind and gracious host, arranged for his colleagues to become commissioned into the Kentucky militia. Through Arno's persuasion, his colleagues were actually commissioned as Honorary Kentucky Colonels, the highest honor awarded by the Commonwealth to serve as Kentucky's ambassadors of goodwill and fellowship around the world.

Among Spatola's honors and awards were the 2002 Kentucky Science and Engineering Foundation Research and Development Award and a 2003 President's Award for Outstanding Scholarship, Research, and Creativity from U of L. Dr Spatola was a founding member of the American Peptide Society, was serving as Secretary, and was a member of the American Chemical Society. He was a co-chairman of the 1990 Gordon Research Conference on Chemistry and Biology of Peptides. He also served on the editorial boards of the Journal of Peptide Research and

Letters in Peptide Science and was an ad hoc reviewer for the National Institutes of Health.

In addition to Dr Spatola's academic career, he founded Peptides International in 1983 as an outgrowth of his research interests. The impetus behind Peptides International's creation was to address the need for automated peptide synthesis and products and services related to it. Arno realized the need for such research support services in the early 1980s, as well as, the need for reliable suppliers for high quality amino acid derivatives, reagents, and resins of solid-phase peptide synthesis (SPPS). The company originally targeted the solid-phase synthesis instrument market, offering the PI-1000 synthesizer, but later focussed efforts on peptide-based biochemicals, resins for SPPS, and custom synthesis services.

The first year at Peptides International was truly eventful. In search of the highest quality peptide reagents and chemicals, Dr Spatola began an alliance to distribute the fine products of the renowned Peptide Institute of Osaka, Japan, then under the direction of its President, Dr Shumpei Sakakibara. This was the beginning of a mutually prosperous relationship that continues to this day, thanks to the ongoing support of Dr Terutoshi Kimura, the Peptide Institute's current President.

During the first year of business, Peptides International's initial customers were an exclusive group of prominent researchers from the peptide community. The remainder of the 1980s saw rapid expansion for Peptides International with the addition of a production laboratory that first produced MBHA resins and penicillamine derivatives. Boc-amino acid derivatives were the most popular selling products at that time. Peptides International became the sole United States distributor for the Peptide Institute of Osaka, and Jackie B. Spatola joined her husband, Dr Arno Spatola, as the company's Controller.

Peptides International's newsletter, PEP-NET, first introduced in 1987, has served as the company's PEPticle communication NETwork to help broaden the scope and quality of the rapidly expanding field of peptide research. Arno's vision was that quality products, expeditious service, a professional staff, and PEP-NET, together, would serve as the distinguishing hallmarks of his company. In 1996, PEPNET.COM was officially launched as the company's web site to continue this peptide information network.

Peptides International's prosperity continued into the 1990s. During this time, the company received its first, and the first-ever in Kentucky, Small Business Innovative

Research Grant (SBIR) Phase I from the National Science Foundation (NSF) for affinity membranes as a solid support for peptide synthesis. In 1993, PI received its first National Institute of Health (NIH) SBIR Phase I grant. Later that year, the company moved into its current, expanded location.

The decade of the 1990s saw additional growth at Peptides International. In 1992, several collagenase inhibitors from Dr Spatola's University research were successfully licensed from U of L through Research Corp Technologies in Tucson and commercialized by PI. Later, Peptides International's product line benefited from several new additions and most notably from exclusive licensing agreements on two key products: CLEAR resins from the University of Minnesota and TAPI (MMP inhibitors) from Research Corp Technologies. Hallmarks of the PI product line include custom designed glassware for SPS, resins, and custom synthesis. These products have become very important to the overall growth of the company and are the basis for successful ventures in the first part of the new century.

By the turn of the century, Peptides International's superior reputation for delivering, producing, and distributing the highest quality products and services had earned record sales in each sequential year. Also, at this time, Peptides International was awarded its second NIH SBIR Phase I grant for a derivative of its highly successful CLEAR resin for facile disulfide formation of peptides, termed CLEAR-OX™.

When Arno was asked how he could meet his extensive obligations at the University and the company, he would simply explain that he hired people to run the company independently of him and secondly, he scrupulously maintained separation between the two activities. From PI's inception, all of the products were to be the best of their kind available. Dr Spatola was proud of his company's solid principals based on research integrity and social responsibility. He believed in supporting the arts and the environment, as well as treating people with respect and kindness. Arno believed in the golden rule: *Do unto others, as you would have them do unto you*. Peptides International's motto, which still holds true today, is to supply the world's best peptide-related compounds in a fast and courteous fashion.

Arno's intense interest in combichem research and drug design efforts was evidence of his sense of duty and purpose. Arno desired to use his talents for a greater end. He believed that research could yield answers, treatments, and cures for serious diseases. Arno always

kept in mind and often reminded others that there is a sense of urgency in research, and all problems have solutions.

Arno realized the potential impact Peptides International could have on the local and global community, as well as the potential for his company's contribution to the advancement of peptide science. He once stated, 'My company is only the tip of the iceberg'. Arno was once quoted as saying, 'Louisville in a sense is strategically located although we do not have a major pharmaceutical company *located here yet*'. Arno believed fervently that the surrounding region was rich in opportunity with the University serving as the main vehicle to drive the growth of health-related companies. Arno was proud to call this his *old Kentucky home* but he would always remain true to his Italian heritage. He would speak fondly of his days in Albany and Arizona and would tell the tales of his travels, domestic and abroad. Part of the company's name 'International' was truly inspired by his journeys abroad to scientific meetings and the realization that research was not limited by geographical boundaries.

In fact, during his many travels, lectures, and every day journeys, Arno would be remembered explaining that peptides are 'short chains of amino acids strung together like box cars in a train'. While he instructed over 5000 students during his tenure at U of L, he had a personal mission to educate every person he encountered about peptides, even the famous jockey, Pat Day, in a hotel elevator in Osaka, Japan.

Like so many of his colleagues, Arno was optimistic, with good reason, about the future of peptide science. Arno shared the vision of many of his esteemed colleagues who all realized peptides were on the cutting edge of many discoveries and eventual cures and treatments. Peptides were once thought of as poor pharmaceutical agents. Realizing this was not always true, Arno began a quest to open people's minds to the reality of the peptide market. His most requested slide was entitled, 'Peptides are not suitable as drugs, a few exceptions...'. In a time before the widespread use of the Internet, when annual sales figures were not available in under 10 s, Arno pooled his resources and called and e-mailed his friends and colleagues around the world to gather sales data of peptide-based drugs (see Table 1). Currently, with improved methods of synthesis and alternative modes of drug delivery, the market for peptide-based pharmaceuticals has come to fruition and is expected to continue to grow.

**Table 1. Peptides are not suitable as drugs, a few exceptions...**

Peptide/protein drugs on the market		
Peptide	Use	1994 world sales (estimated)
Insulin	Diabetes	\$1800M (1995)
ACTH	Diagnostic; multiple sclerosis	\$10M (1995)
Oxytocin	Uterine contraction	\$5M (1995)
Vasopressin and analogs	Antihypertensive	\$95M (1995)
Cyclosporine	Immune suppressant	\$813M (1995)
Octreotide	Antisecretory	\$228M (1995)
Leuprolide	Prostate anticancer	\$650M (1995)
Buserelin	Prostate anticancer	\$150M (1995)
Nafarelin	Prostate anticancer/endometriosis	\$20M (1995)
Captopril	Antihypertensive	\$1177M (1995)
Angiotensin II	Anticancer	?
Histrelin	Precocious puberty/anticancer	?
Goserelin	LH-RH hormone	\$344M (1995)
Thymopentin	Immunomodulator	\$100M (1995)
Calcitonin	Calcium regulation	\$800M (1995)

Taken from Prof. Arno F. Spatola's slide presentation, with permission.

As the field of both peptide research and solid-phase synthesis has grown to include researchers from diverse disciplines, the peptide community represents a portion of Peptides International's customer base. With great pride, Arno insisted that certain milestones in the peptide field be featured in PI's PEP-NET newsletters to promote awareness for these accomplishments. A few notable PEP-NET articles headlines include 'Solution Methods Used for 121 Amino Acid "Peptide" Synthesis', 'Total Synthesis of GFP Achieved!' and 'APS Membership Over 700'. When the American Peptide Society had just begun, the 1990 Summer issue of PEP-NET, proudly endorsed the Society and encouraged others to join, especially scientists in countries without an official Society. At the time, founding members believed membership would exceed 1000 within a year, and like Arno, envisioned an eventual international group, comprising a Federation of existing societies.

Arno did not see a difference between teaching and research or that being a mentor was different than serving as

the CEO of a company. His objective clearly was to provide a fruitful environment for his company to grow and to nourish the growth. First and foremost, Arno would want to be remembered as a *teacher*, as his long-time friend and colleague, Dr Richard Baldwin stated while remembering him. As for one word that best described Arno, most would agree it was *passion*. Arno was passionate about Jackie, Kimberly (his daughter), family, people, children, his Italian heritage, food, peptides, wine, chemistry, the arts, the opera, desserts, Peptides International, IMD<sup>3</sup>, basketball, U of L, upstate New York, friends, pizza, football, colleagues, chocolate, the American Peptide Society, all the peptide Societies, Sigma Xi, ACS, travel, research, integrity, loyalty, and friendship. In short, Arno had a passion for life!

With all the success that Peptides International has enjoyed over these many years, now in 2003, the company is facing sadness in the death of its founder, Dr Arno F. Spatola. The company is now honoring Dr Spatola during its 20th anniversary. Since July, the company members, all of whom were chosen by Dr Spatola, with some mentored by him as peptide scientists, look for comfort in knowing that Dr Spatola lives on in those who knew him. The

long-standing staff will greatly miss the inspired leadership that Dr Spatola afforded Peptides International. However, the company is assured in knowing that Dr Spatola's dedication to excellence over the last two decades has built a strong foundation upon which to further his work and to grow even stronger. Peptides International looks forward to the challenges that the next year, and even the next 20 years, will bring.

In the words of Sir Isaac Newton, often reiterated by Arno, if we have seen further it is by standing on the shoulders of giants. Peptides International proudly remembers Arno F. Spatola for his contributions to peptide research and to the company. We thank him for allowing us to stand on his shoulders and challenging all of us to go even further than we can ever hope to see.

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