

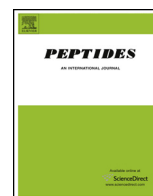


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Festschrift for Dr. Abba Kastin

Endocrine approaches to treatment of Alzheimer's disease and other neurological conditions

Part I: Some recollections of my association with Dr. Abba Kastin: A tale of successful collaboration

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It is a privilege to contribute an article to the Festschrift honoring Dr. Abba J. Kastin for his 35 years of service as the Editor-in-Chief of the journal *Peptides* and for his enormous contributions to the field. However, in my case it is an exceedingly difficult task to adequately express a fitting recognition of my fruitful collaboration and close friendship with Abba that has existed for more than 50 years. My formal association with Abba started in 1964 when he joined my laboratory at the New Orleans VA hospital and Department of Medicine of Tulane University in New Orleans. I believe it would not have been possible to find a medical investigator with a comparable education, training, intelligence and pleasant personality such as Dr. Abba Kastin. His other assets included an excellent knowledge of endocrinology, experimental and clinical research approaches, and his ability for excellent planning and systematic organization.

Dr. Kastin joined my group at the suggestion of Dr. Griff Ross of NIH, an outstanding endocrine clinician and one of the leaders of the Endocrine Society, to work on the search for the substances controlling the release of MSH. This was the only pituitary hormone the release of which was not being investigated elsewhere, and since my laboratory at that time already had a reputation for work on peptide hormones we headed in that direction. Subsequently with our exciting research program and hard work we succeeded in making many notable findings in endocrinology, and neuroendocrinology and we reported them in the various top level journals in the field.

The total number of joint publications (articles, abstracts, reviews and book chapters) with Dr. Kastin for that period amounted to about 322 of which some 76 were for MSH and its release. This was Dr. Kastin's original project, and then he continued on work which led to the subsequent discovery of MSH release-inhibiting factor, the tripeptide MIF-1, in my laboratory.

It may be important to mention that our collaborative clinical publications on hypothalamic hormones involved TRH [2,13,14,30]. Our initial clinical publications on TRH were with my

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collaborator at Tulane University in New Orleans, Dr. Cy Bowers, as the leading author, and myself. Dr. Carlos Gual and Abba Kastin were co-authors [2,13,14,30]. These studies on TRH have been cited in our various book chapters [30].

More than 100 joint publications with Abba were concerned LHRH and its agonistic and antagonistic analogs. Many of these papers were of clinical studies on LHRH which we carried out mostly in Mexico, at the enthusiastic invitation of and in collaboration with Dr. Carlos Gual, Dr. Arturo Zarate, Dr. Gonzales Barcena and others [26,43,47–52,92]. Other publications consisted of major articles, both basic and clinical, on LHRH and on which Abba was a co-author [71]. Other joint publications, mostly clinical, were devoted to somatostatin and its analogs, on which we worked, mostly in England, with Drs. Reg Hall, Mike Besser, M. Thorner, Steve Bloom, and Antonio Gomez-Pan [1,9,10,18,60,89]. In later publications on somatostatin analogs we collaborated with Dr. Gonzalez-Barcena [27,28].

This favorable situation and so many publications on hypothalamic hormones were of course due to our fruitful work on TRH [2,13,14,30]. There was also the issue of our clear leadership in the chemical, physiological and clinical advances on LH-RH [26,43,47–51,72,90,93]. Dr. Kastin's work on MIF and MSH established his leading position in the fields of both MSH and MIF, as he was the first to show that a hypothalamic peptide could act "upward" on the brain, as we had previously shown for hypothalamic peptides acting "downward" on the pituitary [40–42,45,46].

As a result of realizing that peptides could act "upward" on the brain, Dr. Kastin became very interested in the behavioral and CNS effects of hypothalamic hormones and related compounds such as endorphins and enkephalins and so he started elaborate studies on the influence of our synthetic TRH, LHRH, somatostatin, and their analogs, on the brain [46]. As mentioned above his work with MSH was the first to show that any peripherally generated peptide could have direct effects on the brain. Abba carried out both basic

and clinical work on behavioral effects of MSH, with Curt Sandman and Lyle Miller [37,38]. Then he accomplished elaborate CNS studies on MIF, LHRH, Met-enkephalin (also called opioid growth factor) and somatostatin, with Nick Plotnikoff and Rudolph Ehrensing [20,44,62,63]. He also investigated various opiate peptides with Gayle A. Olson and Richard D. Olson [36,39,45], with whom he introduced the concept of endogenous brain anti-opioids. With Jim Zadina he described the naturally occurring, highly selective, high affinity Mu-opiate receptor agonist endomorphin; their original paper in *Nature* [92] has now been cited almost a thousand times. We also examined, with Bill Banks, penetration of somatostatin analogs through the blood–brain barrier [6]. These studies resulted in numerous publications and established Abba as a top expert in this field also. In particular, it was important conceptually to show that a peptide injected peripherally could have an effect on the brain, and then to show that this occurred by its passage directly across the blood–brain barrier. These, now well-established concepts were initially as controversial as that of my own work on control of pituitary function by hypothalamic peptides.

I also collaborated with Prof. Gyula Telegdy and Prof. L. Vecsey from the University of Szeged, Hungary on CNS effects of a hypothalamic MSH analog and other peptides synthesized in our laboratory [84,85].

This collaboration on CNS effects of peptides with Abba Kastin, and later Gyula Telegdy, turned out to be not only important and influential but also exceedingly useful for my future work when I decided to investigate, in my current laboratory, the effects of our antagonistic analogs of growth hormone-releasing hormone (GH-RH) in experimental models of Alzheimer's disease. This decision was made on the basis of our discovery of anti-inflammatory and antioxidative effects of GHRH antagonists and the potential for applying these in the CNS. I will always remain deeply grateful to Dr. Kastin and Prof. Telegdy for introducing and exposing me to these investigations of CNS effects of peptides.

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