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Introduction

Interdisciplinary tryptophan research and its coherence in 2006

Katsuji Takai *, [1]

Ex-Professor: The Department of Medical Chemistry, The Institute of International Health, The University of Tokyo Graduate School of Medicine, Tokyo, Japan

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"The Interdisciplinary Conference on Tryptophan and Related Substances: Chemistry, Biology, and Medicine", a volume of the International Congress Series (ICS), is the proceedings of the eleventh meeting of "The International Study Group for Tryptophan Research (ISTRY-2006 Tokyo)", which was held from July 3 to 7, 2006 in The University of Tokyo, Japan. Over the past three decades, ISTRY has triennially updated topics and paradigms on versatile aspects of tryptophan, one of the unique aromatic amino acids that draw attention in many fields of biosciences. In the last millennium, though each expertise achieved an extensive development, the entirety stood just before coherent understandings. Clearly, this decade is just right to allow a current overview of research on a single amino acid towards understanding of our life system as a whole. Near the end of the last millennium, an amazing discovery was achieved on the chemical/physical forces related to aromatic amino acids, such as tryptophan (Trp), tyrosine (Tyr), and phenylalanine; they are not mere larger-sized hydrophobic amino acids, but each amphiphile subserves "an anion" in the hydrophobic environment to interact with alkaline metal/organic cations, in active/

* Tel./fax: +81 3 5920 4161.
E-mail address: k38takai@nyc.odn.ne.jp (K. Takai).
[1] The President of the Eleventh Meeting of International Study Group for Tryptophan Research (ISTRY-2006) 1-27-1-911 Wakagi, Itabashi-ku, Tokyo 174-0065, Japan.

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modulator sites of catalytic/binding and channel proteins, or to prime the folding of nascent peptides with basic residues. The general, strong, non-covalent force referred to as "cation–π interaction" opened a new vista along with the conventional chemical forces such as hydrogen bondings, salt bridges, and hydrophobic interactions. The proceedings of ISTRY-2006 Tokyo start with the cation–π interaction as the cutting edge of not only aromatic chemistry but also a new molecular basis of life. Among amino acid residues, Trp occupies ~1%, but in the active/binding sites and membrane channels, it is over expressed and one quarter of these Trp appear to be implicated in cation–π interaction. It is a good time to try to explain versatile chemical aspects of Trp coherently by a cation–π interaction, an organizing element, a hydrogen donor, a Lewis basic donor, and an amphipathic nature. In the appealing field of structural biology and dynamics of ion channels, an ammonium channel is updated and discussed with special reference to highly conserved Trp 148, which exerts a critical role supported by a cation–π interaction in the periplasmic vestibule before transversing ammonia through the transmembrane channel. Diverse hierarchies of posttranslational modifications of the Trp residues do exist in proteins; some may be an outcome of one-to-one modification but others derive from two matching reactions like in nitro Trp/Tyr paradigms between unequal states of "modified Trp/Tyr residues/distinct local dielectric constants" vs. uniform levels of free reactants induced by serial signal transductions. Regardless modifications of Trp/Tyr, including nitration/oxidation dramatically change the physical/chemical properties, including cation–π interactions. The paradigm must show something soon in the near future. The stereoselective organic syntheses of active Trp secondary metabolites such as tetrahydro-β-carboline alkaloids, again attract our attention. Trp metabolites/derivatives tend to elicit unique biological/pharmacological activities implications by inherent aromaticity and cation–π interaction at least in part, and a revival to more coherent pursuits by newer syntheses/assessments with mutation, crystallography, and structural matching by computer analyses. The Trp secondary metabolite, indirubin, an active ingredient of a traditional Chinese medical recipe of Danggui Longui Wan, is an appealing model for the syntheses of anti-tumor drugs, since the targets of this "bisindole" are protein tyrosine kinases (PTKs) involving cellular signal transductions. For chronic myelocytic leukemia this acts not only on cyclin-dependent kinases but also on other multiple targets, explaining an avoidance of the appearance of indirubin-resistant cells that is the main drawback of Imanitib, a specific to PTKs, the Able and Src. The ISTRY first experienced the Trp permeases I/II in yeast and Trp auxotroph in a huge hydrostatic pressure with paradigms on intriguing genetic links, dynamics of membrane/Trp permeation, and cell cycles each coupled coherently. The data of the X-ray analysis for indoleamine 2, 3-dioxygenase (IDO), one of the ring-cleavage enzymes of Trp metabolism, is not only for elucidation of heme–tryptophan–oxygen paradigms, but also for providing modulatory sites and IDO inhibitors of immunopotentiators and other uses. To consider paradigms in the central nervous system (CNS) with heterogenous distribution of matters and functions, a pioneer of neuroanatomy for serotonin (5-HT) neurons is invited to define in detail these representative diffuse modulatory systems with at least fourteen 5-HT receptors in the CNS. The 5-HT neurons start from dorsal and median raphe clusters, both in the brainstems where ascending/descending paths cross react, and each projects efferently in mostly non-overlapping manner to the cerebral cortex/basal ganglia and limbic forebrain/midbrain, respectively, as modulatory neurons to form the contacts with other modulatory/