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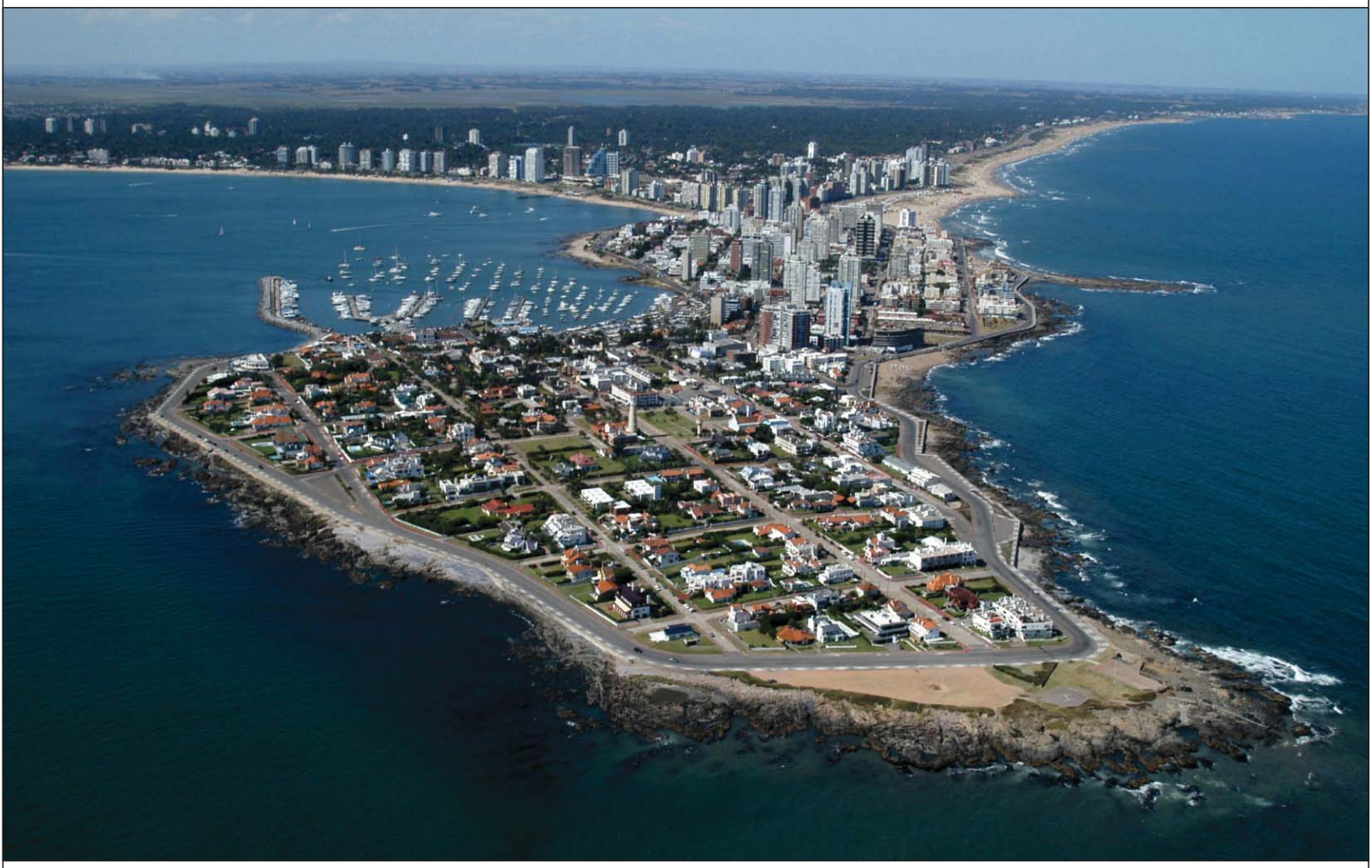

María H. Torre and Dinorah Gambino (Eds.)

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Ni(II) binding to 429-460 peptide fragment from human toll-like receptor (hTLR4)

Zoroddu, M.A.[1]; Peana, M.[1]; Medici, S.[1]; Solinas, C.[1]; Potocki, S.[2]; Kozlowski, H.[2]

[1]*Department of Chemistry and Pharmacy, University of Sassari, Sassari, Italy*
[2]*Department of Chemistry, University of Wroclaw, Wroclaw, Poland*
zoroddu@uniss.it

Contact allergy, commonly induced by nickel, is the most frequent cause of contact hypersensitivity in industrialized countries, with 30% of population being affected. Ni(II) seems to trigger an inflammatory response by activating human Tool-like-Receptor 4 (hTLR4). Species-specific activation, as in this case, required distinct sequence motifs that are present in human but not in mouse, a species not sensitive to nickel-induced allergies. The specific region of human TLR4 responsible for nickel responses could be a sequence containing three histidine residues, H_{431}, and the non- conserved H_{456} and H_{458}, localized in the C-terminus. It has been proposed that the imidazole side chains of the histidine residues H_{456} and H_{458} provide a potential binding site for nickel because they were located at an optimal distance to interact with Ni(II) ions, whereas H_{431} was further apart. We decided to verify the possibility of metal binding to $FQH_{431}SNLKQMSEFSVFLSLRNLIYLDISH_{456}TH_{458}TR$ sequence, containing the three histidines supposedly involved in nickel response, in order to study the binding properties of the peptide fragment and on the thermodynamic stability of its metal complexes. Formation equilibria of Ni(II) complexes have been investigated in aqueous solution and in a wide pH range. Protonation and complex-formation constants have been potentiometrically determined; complex-formation models and species stoichiometry have been checked by means of UV-Vis absorption and CD spectroscopy and investigation through NMR is currently being carried out. The predominant species for a 1:1 peptide/Ni(II) molar ratio was obtained at physiological pH and showed an effective binding of the metal to the target sequence.