

Molecular Basis for Antitumor Effect of Actin-aplyronine A Complex

Kunio Hirata^a, Shin Muraoka^a, Kiyotake Suenaga^b, Hiroshi Tanaka^c, Masaki Yamamoto^{a,d}, Masaki Takata^{a,e}, Hideo Kigoshi^b,
^a*JASRI/SPring-8*. ^b*Dept. of Chemistry of Tsukuba univ.* ^c*Dept. of materials science of Shimane Univ.* ^d*RIKEN/SPring-8*. ^e*CREST/JST*.
E-mail: hirata@spring8.or.jp

Aplyronine A is a promising candidate of anticancer agent isolated from *Aplysia kurodai*. The complex structure of actin-aplyronine A is determined via a synchrotron X-ray analysis at 1.45 Å resolution. Aplyronine A binds to actin in the similar manners with the trisoxazole toxins and gelsolin segment I around its aliphatic tail part which should play an important role for F-actin depolymerizing activity. In contrast, the structural aspects relating to peculiar interactions between aplyronine A and actin can be found around the macrolide ring part which should be a key to the potent antitumor effect of aplyronine A. Actin-aplyronine A complex structure should suggest that each complex comes to have ability to effect other biological reactions which are essential for deaths of cancer cells. The precise charge density map was also visualized with the maximum entropy method to construct the structure model of a disordered stereoisomer of a peculiar side-chain of aplyronine A as well as to visualize ambiguous bonding electrons between aplyronine A and actin.

Keywords: aplyronine A, antitumor effect, maximum entropy method