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Conference Committee

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Abstracts

LECTURES - MARCH 13

POLYMER CARRIERS FOR TARGETED DRUG DELIVERY AND CONTROLLED DRUG RELEASE

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Nondegradable *N*-(2-Hydroxypropyl)methacrylamide (HPMA) copolymers or biodegradable poly(ethylene glycol) (PEG) multiblock copolymers conjugated with antibodies were designed as water-soluble carriers of anticancer drugs facilitating site-specific therapy. High-molecular-weight polymer carriers were used for passive targeting to solid tumors while conjugates with specific polyclonal or monoclonal antibodies were designed for specific delivery of anti-cancer drug doxorubicin to tumor cells or model tumors inoculated in mice. Doxorubicin conjugates targeted with B1 monoclonal antibody (mAb) were shown to possess strictly tumor-specific binding capacity to target BCL1 cells *in vitro* and superior *in vivo* activity to free doxorubicin or non-targeted polymer drug in the treatment of established BCL1 leukemia in mice. Likewise, the use of conjugates targeted with anti EL4 mAb resulted in large amount of long-term survivors after treatment of mice bearing mouse EL4 lymphoma. Preliminary evaluation of doxorubicin conjugate in human demonstrated that the polymer drugs rank among the most promising candidates for successful application in human cancer chemotherapy.

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LECTURES - MARCH 14

INTERACTION OF RHOA GTPASE WITH ITS EFFECTOR P160ROCK

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The GTP-binding proteins (or Rho-GTPases) of the Rho-family regulate a variety of cellular processes in all eukaryotic cells, ranging from cytoskeletal reorganization and cell motility to gene transcription in response to external stimuli [1]. To date, 19 different mammalian Rho-GTPases have been identified from which Cdc42, Rac1 and RhoA are the most extensively characterised members of the Rho-family. The function of Rho-GTPases depends on the guanine nucleotide-bound state. As molecular switches Rho-GTPases cycle between an inactive GDP-bound state and an active GTP-bound state, which is controlled by numerous cellular proteins. Active form of Rho-GTPases interact with their downstream targets, so-called effector proteins, that are responsible for the diverse biological effects of Rho-GTPases [2]. One of the best studied Rho-Effectors, the Ser/Thr kinase p160Rock, plays a key role in actin-myosin filament assembly by activation of signalling molecules involved in various biological processes [3].

We will present the structure of the complex of RhoA GTPase with the Rho-binding domain of p160Rock. We found that the switching regions of RhoA molecule interacts with C-terminal part of parallel coiled-coil formed by Rho-binding domains. Such an arrangement of the complex will be discussed with respect to the general switching mechanism of GTPases and their interaction with downstream effectors.

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2. A. L. Bishop & A. Hall, *Biochem J.* **348** (2000) 241-255.
3. M. Amano, Y. Fukata & K. Kaibuchi, *Exp Cell Res.* **261** (2000) 44-51.