Protein Kinase CK2: new perspectives of an old kinase

Design of specific small molecules that are able to block (inhibit) function of macromolecular targets responsible for the development of certain disorder is the “classic” and most widely used approach in modern drug therapeutics, e.g., in cancer treatment.

To what criteria the cancer drug target must correspond before it could be accepted as a promising object for searching of an appropriate anticancer drug? Ideally it must be:

(i) disfunctioned in cancer cells;
(ii) essential for cell surviving (target “switching-off” must lead to cell death); and
(iii) target’s activity must not be compensated by other macromolecules;
(iv) the target must be presented only in tumour cells

Surprisingly, Protein Kinase CK2 corresponds to three out of four criteria indicated above.

Since 2005 this kinase was generally accepted as pharmacological tool of proven high therapeutic value. The oncogenic potential of protein kinase CK2 and its involvement in virally mediated pathologies and inflammatory disorders has led to an increasing number of studies aimed at the discovery of selective CK2 inhibitors.

Novel, efficient at low micromolar concentrations, and selective CK2 inhibitors [1-7] has been recently designed by OTAVA Ltd., a leading Ukrainian company.

To discover new inhibitors, company’s researchers spanned computer-based molecular modeling with chemical synthesis of compounds which were further tested in vitro to investigate their ability to bind to and affect the activity of CK2. The binding modes of inhibitors that target the ATP-binding site of CK2 were also studied.

Some recently discovered novel patent-free inhibitors were organized in clusters of similar compounds: **ProHit™ Compound Sets**. Currently, OTAVA Ltd. exclusively offers **ProHit™ Sets of CK2 inhibitors** to academic and commercial laboratories worldwide to use in drug discovery programs targeting protein kinases. The company also plans to extend **ProHit™ Sets** to other protein kinase targets.

List of selected publications by OTAVA’s scientists:

[1] Evaluation of 4,5,6,7-tetrahalogeno-1H-isoindole-1,3(2H)-diones as inhibitors of human protein kinase CK2. Golub AG, Yakovenko OY,

Prykhod'ko AO, Lukashov SS, Bdzhola VG, Yarmoluk SM. *Biochim. Biophys. Acta*. **2008**, 1784, 143.

[2] Kirchhoff atomic charges fitted to multipole moments: implementation for a virtual screening system O.Ya. Yakovenko, A.A. Oliferenko, V.G. Bdzhola, V.A. Palyulin, N.S. Zefirov. *J. Comput. Chem.* **2008**, 29, 1332.

[3] Evaluation of 3-Carboxy-4(1H)-quinolones as Inhibitors of Human Protein Kinase CK2. Golub AG, Yakovenko OY, Bdzhola VG, Sapelkin VM, Zien P, Yarmoluk SM. *J. Med. Chem.* **2006**; 49, 6443.

[4] Evaluation of 4H-4-chromenone derivatives as inhibitors of protein kinase CK2. A.O. Prykhod'ko, O.Ya. Yakovenko, A.G. Golub, A.G. Bdzhola, S.M. Yarmoluk, *Biopolymers and cell* **2005**, 21, 287.

[5] Search for protein kinase CK2 inhibitors among 3-carboxy-4-aminoquinoline derivatives. V.M. Sapelkin, A.G. Golub, O.Ya. Yakovenko, V.G. Bdzhola, S.M. Yarmoluk, *Ukrainica Bioorganica Acta* **2005**, 2, 28.

[6] Search for kasein kinase 2 inhibitors among 4 aminoquinazoline derivatives. V.M. Sapelkin, A.G. Golub, O.Ya. Yakovenko, V.G. Bdzhola, S.M. Yarmoluk, *Ukrainica Bioorganica Acta* **2004**, 1, 74.

[7] Inhibitors of protein kinase CK2. A.O. Prykhod'ko, G.G. Dubinina, S.M. Golovach, S.M. Yarmoluk, *Ukrainica Bioorganica Acta* **2004**, 1, 39.

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