إضافة مقترح بحثي جديد لمقرر 600 كيح

* Title of the proposed project in Arabic - عنوان المشروع باللغة العربية

بكل 2 الطاقة الملزمة والسمية الخلوية للأبتامرات العلاجية المضادة للسرطان

Title of the proposed project in English *

Bcl 2 binding energetics and cytotoxicity of therapeutic anticancer aptamers

* PI - المشرف الرئيس

Gouse M. Shaik

* Specialty of PI - التخصص الدقيق للمشرف الرئيس

Immunology

* Co-PI - المشرف المساعد

Md. Ashrafuzzaman

المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات العليا (بالشهور) - Expected time in month to finish *

11

Abstract of the proposal (No more than 200 words) *

We have designed a set of nucleic acid aptamers using an information-driven entropic fragment based approach (EFBA) [1,2] to target anti apoptotic Bcl 2 protein. This will lead us towards developing therapeutic drugs targeting apoptosis in cancer treatment. In this project we will use our designed aptamers to address the Bcl 2 binding energetics using in silico numerical computations (NCs) [3]. NC will help us address the Statistical binding phenomena and let us obtain binding energy related parameters.
Cytotoxicity of in silico validated aptamers will be tested on selected cancer cell lines (breast or liver cancer) using MTT assay or trypan blue exclusion method. Anti metastatic properties of aptamers will also be tested using invasion assay or scratch plate assay. Thus we shall evaluate the therapeutic potential of the selected novel aptamers which shall lead us planning for future in vivo studies.

Hypothesis of the proposal *

Aptamers are designed considering biophysical properties of Bcl 2 protein structure, so are target specific.
The aptamers will show statistical binding to Bcl 2 structure with stable energetics.
Inhibiting the function of Bcl 2 can have positive outcomes in cancer treatment.
Proapoptotic and antimetastatic ability of Bcl 2 aptamers will be assessed through cytotoxicity and migration in selected cancer cell line.

Specific objectives *

1. Understand the Statistical Bcl 2 binding energetics of designed aptamers
2. Culture breast cancer or liver cancer cell lines
3. Evaluate cytotoxicity of Bcl-2 aptamers
4. Evaluate antimetastatic ability of Bcl-2 aptamers

Methodology & Major Techniques to be used *

In silico aptamer-Bcl 2 binding energetics will be assessed using numerical computation, one component of our patented direct detection method, see refs. [3]. Programming language Mathematica 10 (or the latest version of it) will be used to create the computational template.
Standard cell culture methods.
MTT assay [4] or counting trypan blue exluded cells using hemocytometer will be employed to assess cytotoxicity.
Migration of cells as a measure of metastasis will be tested using invasion assay or scratch plate assay [5,6].

Availability of Samples *

- (●) Yes
- ( ) No

Kindly justify *

Availability of Chemicals *

- ○ Yes
- ◉ No

Kindly justify *

Once the theoretical design and computational binding assays parts are done a few chosen aptamer candidates and media additives and kits will be required for purchasing (if student finds her/his own finance from department or other granting agencies or elsewhere including personal ones). Cost is approximately 12,000 SAR. Mathematical program will be required to get installed in student's computer/laptop. Cost is approximately 550 SAR.

Availability of Instruments *

- (●) Yes
- ( ) No

Ethical Approval *

- ( ) Ethical approval is available
- (●) Not needed
- ( ) In the process

Recent References *

[1] C-Y. Tseng, Md. Ashrafuzzaman, J. Mane, J. Kapty, J. Mercer, J. Tuszynski, Entropic fragment based approach to aptamer design. Chem Biol Drug Des (2011) 78, 1-13, cover page of the issue
[2] Md. Ashrafuzzaman, C.-Y. Tseng, J. Kapty, J. Mercer, J. Tuszynski, A computationally designed DNA aptamer template with specific binding to phosphatidylserine, Nucleic Acid Therapeutics (2013), 23, 418-26.
[3] Md. Ashrafuzzaman, C.-Y. Tseng, Patent US 9529006 B1. Link: https://www.google.com/patents/US9529006
[4] Mosmann, T. (1983) Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays, J Immunol Methods 65, 55-63.
[5] Kleinman, H. K., and Jacob, K. (2001) Invasion assays, Curr Protoc Cell Biol Chapter 12, Unit 12 12.
[6] Rodriguez, L. G., Wu, X., and Guan, J. L. (2005) Wound-healing assay, Methods Mol Biol 294, 23-29.