إضافة مقترح بحثي جديد لمقرر 600 كيح

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

توبولين ملزم الطاقة من أبتامرز مصممة وتأثيراتها التنظيمية على التكاثري والأنشطة المنتشر في خط الخلايا السرطانية-α

Title of the proposed project in English *

α-tubulin binding energetics of designed aptamers and their regulatory effects on proliferative and metastatic activities in cancer cell line

* PI - المشرف الرئيس

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* Specialty of PI - التخصص الدقيق للمشرف الرئيس

Biophysics

* Co-PI - المشرف المساعد

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

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

We have designed [1,2] a set of nucleic acid aptamers using an information-driven entropic fragment based approach (EFBA) to target α-tubulin. This will lead us towards developing therapeutic drugs regulating tubulin polymerization in cancer cells. In this project we will use our designed aptamers to address their α-tubulin binding energetics perfoming in silico numerical computations (NCs) [3]. NC will help us address the Statistical binding phenomena and let us obtain binding energy related parameters.
Anti-proliferative effect 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 the structure of α-tubulin, so are target specific.
The aptamers will show statistical binding to α-tubulin with stable energetics.
Aptamer binding with α-tubulin can regulate α- and β-tubulin dimerization, thus affecting tubulin polymerization and cell division.
Antiproliferative and antimetastatic ability of α-tubulin aptamers will be assessed through cytotoxicity and migration in selected cancer cell line.

Specific objectives *

1. To discover therapeutic aptamer candidates for regulating α- and β-tubulin dimerization.
2. Aptamer efficacy on tubulin polymerization will be assessed in selected cancer cell lines through cytotoxicity measurements.
3. Testing the antimetastatic potential of aptamers

Methodology & Major Techniques to be used *

For aptamer designing see EFBA [1,2] or Screened Coulomb interaction based approach (SCIBA), see ref. [3].
For in silico and in vitro aptamer-lipid binding energetics, see ref. [3]
Standard cell culture methods.
MTT assay or counting trypan blue exluded cells using hemocytometer will be employed to assess cytotoxicity [4].
As tubulin is essential for maintenance of cytoskeleton we will test the morphological changes induced by anti-tubulin aptamers through microscopy. Also anti metastatic properties of aptamers 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.

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