إضافة مقترح بحثي جديد لمقرر 600 كيح

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

43/5000

تصميم أبتامرز بس لاستهداف موت الخلايا المبرمج

Title of the proposed project in English *

Designing PS aptamers to target apoptosis

* PI - المشرف الرئيس

Md Ashrafuzzaman

* Specialty of PI - التخصص الدقيق للمشرف الرئيس

Biophysics

* Co-PI - المشرف المساعد

Seema Zarger

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

11 months

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

The project proposes an information-driven approach towards developing theranostic (therapeutic and diagnostic) drugs targeting apoptosis in cancer treatment. Our greater objective is to target several biomarkers which are known to indicate apoptosis including phosphatidylserine (PS) externalization. We aim at designing and testing imaging probes with potential applications in the assessment of patients undergoing cancer treatment.
This project has specifically been designed in mainly three steps.
Step I. Design aptamers that bind to PS and phosphatidylcholine (PC) using standard theoretical techniques like screened Coulomb Interaction based approach (SCIBA) or entropic fragment based approach (EFBA). PC is the major lipid on cell membrane whereas PS gets migrated in extracellular region during apoptosis, so is an important biomarker of apoptosis.
Step II. Using direct detection method (for details see our recent patent US 9529006 B1) we shall then perform in silico binding assays on selection of aptamer candidates for PS over PC from binding energetic perspectives. PS binding aptamers will be used for assessing apoptosis while PC binding aptamers as negative control.
Step III. Using direct detection method (for details see our recent patent US 9529006 B1) we shall then perform in vitro binding assays on selection of aptamer candidates for PS over PC. Finally, we shall find best diagnostic aptamer candidates for doing future in vivo studies (not included here).

Hypothesis of the proposal *

Aptamers are designed considering biophysical properties of the structure of PS and PC, so are target specific.
The aptamers will show statistical binding to corresponding lipids PS and PC with stable energetics. The inverse binding should be negligible.
PS aptamer binding to PS and nonbinding to PC will help detect apoptosis.
PC aptamers' non binding to PS will provide negative control platform.

Specific objectives *

1. To discover apoptosis diagnostic aptamer candidates for PS binding during therapeutic anticancer treatment.
2. Testing aptamer efficacy on lipid binding using in silico statistical energetic analysis.
3. Testing aptamer efficacy on lipid binding using in vitro liposome binding potency measurements.

Methodology & Major Techniques to be used *

For aptamer designing see SCIBA (patent filing underway), EFBA (see refs. [Tseng et al., 2011; Ashrafuzzaman et al., 2013]).
For in silico and in vitro aptamer-lipid binding, see refs. [patent US 9529006 B1]

References

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
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.
US 9529006 B1. Link: https://www.google.com/patents/US9529006

Availability of Samples *

- ○ Yes
- ◉ No

Kindly justify *

Partially present. For the rest consider the following
Requirements:
Once the theoretical design (Step I) and computational binding assays (Step II) parts are done a few chosen aptamer candidates and lipids 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. If the funding is unavailable, we shall alternatively use the existing lipids and aptamers (discovered for general lipid binding) in stock to demonstrate the in vitro assay on lipid binding of aptamers. But this alternative route will only let the student understand the in vitro binding techniques for general purposes not related to the designed sequences in this project.
Mathematical program will be required to get installed in student's computer/laptop. Cost is approximately 550 SAR.

Availability of Chemicals *

- ○ Yes
- ◉ No

Kindly justify *

This is a discovery project. Partially present. The rest aptamer sequences that are unknown now will be discovered. Plus also consider 'Requirements' attached in previous section.

Availability of Instruments *

- (●) Yes
- ( ) No

Ethical Approval *

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

Recent References *

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

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