SmartGlucoBinder: Design and Synthesis of Small Glucose Binder Molecule using Computational Intelligence Approach

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Submitted By : Vijay Kumar

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Proposal

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Proposal Details

Project Title :	SmartGlucoBinder: Design and Synthesis of Small Glucose Binder Molecule using Computational Intelligence Approach
Scheme :	Early Career Research Award
Broad Area :	Life Sciences
Sub Area :	Life Sciences(ECR)
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Total Cost (in Rs.) :	*39,57,000*
Name of Principal Investigator :	Vijay Kumar
Email ID :	vijaykumarchahar@gmail.com
Date of Birth :	10-Jun-1982
Contact No :	+917073169619
Category :	GEN
Gender :	Male
Nationality :	Indian
Is differently abled :	No
Designation :	Assistant Professor
Department :	Computer Science and Engineering
PI Address :	Village karamgarh, p.o. sahuwala-1st, sirsa
PI Institute :	Thapar Institute of Engineering & Technology
State :	Haryana
PI Institute Address :	Adarsh nagar, prem nagar, patiala, pb, Patiala, Punjab-147004
Pin Code :	125077
Institute Joining Date :	31 July, 2015

CO PI Details :

Name & Designation	Date of Birth	Mobile No.	Email	Institute Details
Prashant Singh Rana (Assistant Professor)	15-Mar-1982	919313889932	psrana@gmail.com	Thapar Institute of Engineering & Technology, Adarsh Nagar, Prem Nagar, Patiala, PB, PUNJAB-147004
Amjad Ali (Associate Professor)	10-Jun-1978	919569150824	amjadali@thapar.edu	Thapar Institute of Engineering & Technology,

				Adarsh Nagar, Prem Nagar, Patiala, PB, PUNJAB-147004
Avinash Mishra (Post doc research Fellow)	14-Mar-1984	919311618895	avinash.mishra@novoinformatics.com	Indian Institute of Technology Delhi , Hauz Khas, New Delhi, DELHI-110016

Project Summary : Designing good carbohydrate receptors/binders working in aqueous systems remains a great challenge in chemical biology, but one with great implications due to the biological importance of carbohydrates. Glucose levels, particularly, have a role in many disease states, such as diabetes. Therefore, molecules that selectively and reversibly bind to glucose are of great interest for therapeutic purposes.
The major objective is to design and develop a novel homogeneous D-glucose binder that meet the following technical requirements (Davis et al, Nature Chem. 2012, 718) and also based on some chemical compound class with known good drug potential (Stefan Kubik, Nature Chem. 2012, 697).

1. The proposed homogeneous glucose binder must reversibly and non-covalently bind D-glucose in water at neutral pH with association constant (Ka) higher than 100. In other words, the affinity should be stronger than 10 millimolar in terms of the displacement constant, Kd.
•D-glucose exists in aqueous solution in equilibrium between pyranose, furanose and non-cyclic forms. The glucose binder must bind D-glucose at equilibrated conditions. It is not important which glucose form is actually bound, as long as the apparent binding constant at equilibrated conditions meets the above target.
•The binding affinity can be measured by spectroscopic methods (for example glucose titration monitored by UV/VIS or NMR) or by calorimetry or similar methods.
•Binding studies by matrix immobilization (Surface Plasmon Resonance, etc) will not be used here, but immobilization methods can supplement measurements in solution if desired.
2. The proposed small molecule must be synthesised in homogeneous, pure form (95 % purity as measured by HPLC or NMR or similar methods).
3. The glucose binder must be soluble in water at neutral pH (7.4) in sufficient amounts to convincingly demonstrate the glucose binding.
4. The molecular weight must be below 2,000 Daltons. Molecular weights above 2,000 Da are acceptable ONLY if the structure includes solubilizing groups to ensure water solubility, and the core glucose binder has molecular weight below 2,000 Da.
5. The small molecule glucose binder must be colourless or weakly yellow in dilute solutions.

There are more than 40 million (ZINC, PubChem) commercially-available compounds for virtual screening. The goal is to quickly and efficiently test whether certain chemical compounds have the potential to be desired a glucose binder molecule. Physicochemical properties of chemical compounds always guide to determine the activity (active or inactive) of the molecule, therefore it has been rigorously used to classify as drug and non-drug. In this work, we will use computational intelligence approaches (such as random forest, support vector machine, neural network, linear model, etc) with physicochemical properties to design glucose binder molecule.

Objective :

- To design and synthesis a non proteinous small glucose-sensitive molecule and that must be bio-

compatible, non-toxic and independent of environment factors.

• To develop a framework to quickly and efficiently test certain chemical compounds for their probable chances to disrupt processes in the human body.

• To develop better glucose binder assessment features, methods and algorithms along with better data structures to handle the big data.

• To develop a stand-alone and/or web-based application(s) that helps the researchers and research community to design a customize glucose binder.

Keywords : Glucose Binder, Binding Affinity, Diabetes, Machine Learning, Feature Selection

Expected Output and Outcome of the proposal :

• The outcome of SmartGlucoBinder will be available in the form of stand-alone and/or web-based application that help the researchers and research community to design a customize glucose binder.

• SmartGlucoBinder can also be used as a decision support system that helps to improve the activity of glucose binder molecule.