Every breath you take I'll be serving you

Screening of prospective inhibitors for AKT1 and IL-10

Kiseleva Y., Tret'yakov D., Avdiunina P., Antonov G., Vlasov P.

anis.camp@gmail.com

Introduction

Asthma is a common inflammatory disease of the airways of the lungs. It is characterized by variable symptoms, airflow obstruction and bronchospasm. As of 2011 250000-345000 people have died each year from asthma.
We have studied an article about novel candidate genes for asthma.
We chose two genes associated with two proteins which could be potential targets for asthma: AKT1 and IL-10.

Methods and Materials

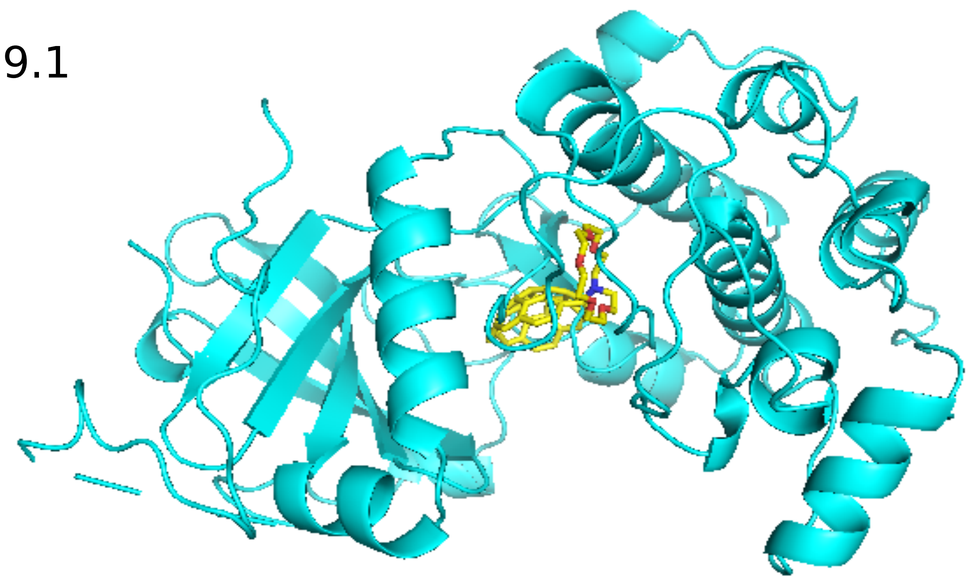
Vina AutoDock tools package has been used to screen NCI compound set vs target proteins to identify the most prominent inhibitors. Target structures have been taken from Protein Data Bank and have been aligned using TM-Align tool for preliminary analysis and for binding site selection.

Aims

- To research for candidate proteins related to the co-morbid conditions of asthma. It can also be useful for identifying new drug targets.
- To learn more about those proteins and their role in asthma and mechanisms of inflammation

Fig 1. Structural alidnment of target receptors

ΔG=9.1



Targets

AKT1 is an enzyme that plays a key role in the PI3K/AKT/mTOR pathway which is directly related to cellular proliferation, cancer and longevity. Many researchers pay attention on its functions because it can be oncogene, but it almost has not been considered as an antiasthma target.
We found one recent research about how AKT1 activation induces Airway Smooth Muscles hypertrophy. Researchers cleaned up that AKT1 in airway myocytes increased protein content per cell and induction of AKT1 activity can promote increased cell size.
This indicates that AKT1 activation can cause ASM hypertrophy. AKT1 can be inactivated by PP2 or PHLPP and by Ipatasertib which is an anti-inflammatory cytokine. IL-10 signals rough a receptor complex consisting of IL-10R1 and IL-10R2.
The results of recent explorations showed diminished level of IL-10 and elevated levels of IL-10 and IL-33 (pro-inflammatory cytokines) in asthmatics (negative correlation).
We have done screening and found one potential ligand for IL-10 - A C60 Fullerene which could be probably used for the treatment of asthma.

Conclusion

Our analysis identifies new antiashma drugs rely on screening methods which involved passively-sensitised mast cells and on airway smooth muscle cell cultures of the animals.
AKT1 and IL-10 may prove to be useful therapeutic targets to prevent or reverse asthmatic ASM hypertrophy and to supress inflammatory processes during asthma which possibility remains to be tested.
Potent compounds can be obtained for free via the Development Therapeutics Program from National Cancer Institute to be tested experimentaly.

References & Acknowledges

Daniil Polyakov - MIPT (Russia) and IST (Austria)
Nikita Gudimchuk - MSU (Russia)
Ilya Mazein - SPbU (Russia)