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Distribution of *CYP2C9* variant genes in the healthy Thai population associated with medical cannabis metabolic pathway

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Medical cannabis consists of tetrahydrocannabinol (THC) and cannabidiol (CBD). *CYP2C9* is a major metabolizer of THC and the frequency of *CYP2C9* genotypes vary between populations worldwide. THC-induced adverse effects (AE) can be explained in terms of *CYP2C9* gene variants in pharmacogenetics. This study aims to investigate the impact of the frequency of *CYP2C9* variants related to THC metabolic pathways in the healthy Thai populationWe have recruited a set of unrelated healthy Thai subjects (n=160). Genotyping for *CYP2C9 (*2 and *3)* were subsequently analyzed through real-time PCR. We found that *CYP2C9*1* alleles is the most common form of the *CYP2C9* gene among the Thai population, comprising a percentage frequency of approximately 95.94%. *CYP2C9*3* alleles were found to occur at only 4.06%. However, *CYP2C9*2* alleles were absent among the subjects. Furthermore, in the aspect of phenotypes and genotypes, we found that the phenotype of extensive metabolizers (EM) (*CYP2C9*1/*1*, wild-type) genes have the highest frequency. Intermediate metabolizers(IM)*(*1*3)* and poor metabolizers *(*3/*3)* were also found from the samples, respectively 6.88% and 0.62%. Our results for *CYP2C9*1/*3* and **3/*3* frequency is also similar to previous studies in Asian populations. The allelic variants *CYP2C9*2* and *CYP2C9*3* have been presented to experience decreased enzymatic activity in the THC metabolism pathway. In conclusion, the distribution of *CYP2C9*3* in Thai populations might be associated with THC-induced serious adverse effects through metabolic pathways.

Keywords: *CYP2C9* gene, Thai population, Cannabis

Biography

I am Bunnalin Liamputhong and I am currently studying in Regent's International School of Bangkok as a senior high school student in the Twelfth grade. I have a strong interest in medicine and aspire to continue my studies in a medical university. An area which I find quite fascinating is pharmacogenetics, hence the reason why I carried out this research.

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Pharmacogenetics Database of Lumiracoxib-induced DILI in healthy Thai population

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Lumiracoxib is a cyclooxygenase-2 inhibitor used mainly for symptomatic treatment of osteoarthritis and acute pain in patients. However, lumiracoxib is responsible for drug induced liver injury (DILI), an injury which has low incidence of occurrence but can cause serious life threatening outcomes. We found the genetic markers predictive of lumiracoxib- related hepatotoxicity in Europeans, consisting of *HLA-DRB1**15:01 (P=6.8x10-25, OR 7.5 and 95% CI = 5.0-11.3). Furthermore, *HLA-DQA1**01:02 is also found associated with lumiracoxib-related hepatocellular injury with a 99.0% NPV and the highest sensitivity of 73.6% from genome-wide studies. Therefore, the distribution of pharmacogenetics markers were explored in the healthy Thai population. The aim of this study was to investigate the frequency of *HLA-DRB1**15:01 and *HLA-DQA1**01:02 associated with pharmacogenetics markers of lumiracoxib-induced DILI in the healthy Thai population. 200 participants in this study were recruited from an unrelated healthy Thai population. *HLA* class II alleles were genotyped using sequence-specific oligonucleotides. Our data revealed 41 alleles of the *HLA- DRB1**15:01 (10.25%) and 98 alleles of the *HLA-DQA1**01:02 (24.50%) in the Thai population. We founded the most allele frequencies are *HLA-DRB1**15:02 (15.25%), *-12:02* (14.25%), *-15:01* (10.25%), *-09:01* (8.75%), and -16:02 (7.50%). Furthermore, *HLA-DQA1**01:01 (27.75%), *-01:02* (24.50%), *-03:02* (13.00%), *-06:01* (10.25%), and *-02:01* (4.50%) in Thais. Similarly in Europeans, there was also a high frequency of *HLA- DRB1**15:01 (6.76%) and *HLA-DQA1**01:02 (15.77%). To conclude, instead of completely withdrawing lumiracoxib from treatments, it is advisory to screen for the pharmacogenetics markers of *HLA-DRB1**15:02 and *HLA-DQA1**01:02 alleles in Thai patients for the purpose of avoiding DILI.

Key Words: Pharmacogenetics database, DILI, Thai population, *HLA-DQA1**01:02, *HLA- DRB1**15:01

Biography

Pantapat Chokpitakkul (Bob) is 17 years of age and studies at Shrewsbury International School, Bangkok. I am currently completing a literature review for publication and preparing an oral presentation for my preparations in applying to medicine in Thai and UK universities. I have an interest in precision medicine in particular, leading me to focus on this research.

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The pharmocogenetics database of *CYP2C19* variant in Healthy Thai population

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CY2C19 is a liver enzyme responsible for metabolizing clinical drugs such as: omeprazole, clopidogrel, phenytoin, proguanil, diazepam, citalopram, imipramine, amitriptyline and clomipramine. In previous studies, the variants of *CYP2C19* can be used to predict the specific reaction a person might have after receiving medicine. The aim of this study was to investigate the variant of *CYP2C19* genes and the allele distribution in the healthy Thai population. *CYP2C19**2 (c.681G>A; rs4244285), *CYP2C19**3 (c.636G>A; rs4986893), *CYP2C19**17 (g.-806C>T; rs12248560) of 160 unrelated healthy Thai individuals were test using real-time PCR. The results show that the most common allele frequency was *CYP2C19*1* with a percentage of 68.44%. The second most common allele frequency was *CYP2C19**2 with a percentage of 23.75%. Lastly, *CYP2C19**3 was found in only 4.69% and *CYP2C19**17 with 3.13%. *CYP2C19* metabolizer in the healthy sample consist of 4 phenotypes: Extensive metabolizers (EM) (*CYP2C19**1/*1 of 45.00% and *CYP2C19**2/*17 of 1.25%), the Intermediate metabolizers (IM) (*CYP2C19**1/*2 of 34.38% and *CYP2C19**1/*3 of 7.50%), the poor metabolizers (5.0% with *CYP2C19**2/*2 and 1.88% with *CYP2C19**2/*3 genotypes), and the Ultra rapid metabolizers (UM: 5.00% with *CYP2C19**1/*17 genotype). The result shows that more than half of the participants have abnormal metabolism with only 46.25% of the participants having normal (extensive) metabolizers. A concerning 41.88% of participants are intermediate metabolizers. Thus, the database of *CYP2C19* variant distribution in the healthy Thai population should be compared with other ethnicity to support precision medicine for screening prior before administration of medication to individuals.

KEYWORDS: Thai population, *CYP2C19* gene variant, Real-time PCR

Biography

I am a year 12 student studying the IB diploma programn in the Regents International School Bangkok. My current interests are medicine and research; precisely pharmacogenetics. I hope to use this opportunity to strengthen my experience inorder to pursue my dream carrer of a doctor.

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Unknown Mutation detection via Restriction hybridization Method instead of using Next generation sequencing method

Umair Masood

In biology mutation is a change in the nucleotide sequences of the DNA of an organism Mainly there are three types of mutation: point mutation, deletion and insertions. Once the mutation has been defined allele specific oligonucleotide hybridization, amplification, heteroduplex formation method referred to as a diagnostic method some advance technique like CRISPR cas9 system is using for selected mutagenesis. Using restriction method system we can detect a mutation. Let's say you have a DNA sample with fluorescent labeled from patient and you want to make sure that gene you are interested is in healthy gene. We can design different short fragment sequences to scan through DNA or find specific gene or mutation. The sequences scan the DNA if the sequences does not find targeted gene it does not bind to it its means that no fluorescence color appears under UV-light each different short fragment sequences is label with different colors. If the different short fragments sequence does not bind to the DNA or specific gene or area this means that there will be no color appear under UV light this part or gene will be separated from the DNA by using Restriction enzyme to do a Sanger sequencing gel electrophoresis. Result of the Sanger sequencing will provide the information about sequence of unknown part or gene of the DNA this method is easier and cost economic method instead of Next generation sequencing method.

Result and observation:

In the given diagram E,G,F does not show any color under UV light its mean that E,G,F part will be separated from the DNA in order to perform a Sanger gel electrophoresis E,G,F have unknown variation or unknown SNP which cannot be available in any Database or data sections

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Assessment of the safety of therapeutic COVID 19 specific T cells using a human skin explant assay for Graft versus Host Disease

Anne Dickinson

Emeritus Professor Newcastle University; CEO Alcyomics Ltd

Here we use a skin explant assay for Graft versus Host Disease (GvHD) prediction to demonstrate that SARS-CoV-2- specific T cells, isolated using SARS-CoV-2 pooled spike, nucleocapsid and membrane peptides give rise to little or no by-stander GvH type reactivity. The Virus-Specific T cells (VST) were obtained using a GMP compliant process and expanded in culture as a potential COVID-19 therapy. (1)

VST were generated from three COVID convalescent donors (plus matched un-manipulated mononuclear cells as responder controls) and tested against three different third party non-matched peripheral blood lymphocytes in a mixed lymphocyte reaction (MLR). After 7 days of co-culture the VST cells and un-manipulated lymphocytes were assessed for T cell proliferation, cytokine release and tested for histopathological damage using autologous skin from the third party stimulator cells in a unique skin explant model used for predicting GvHD (2,3).

For the skin explant assays all three VST isolates showed minimal GvH type reactivity, Grade 1 (n= 15) or Grade II (n=2) compared to un-manipulated source leukocytes (Grade II n= 9) and Grade III (n=8). T cell proliferation responses were significantly lower in the VST cells. Cytokine response analysis is underway.

This indicates that VSTs used for adoptive therapy of COVID-19 infections are unlikely to induce significant GvHD, and therefore this assay may help support the safety profile of new cell therapies.

Biography

Anne Dickinson was a researcher for over 30 years at Newcastle University, where she used human skin based in vitro assays for predicting graft versus host disease (GvHD), work that has been extensively published in over 100 peer-reviewed journals.
Anne founded Alcyomics Ltd, where the technology was modified and patented for predicting adverse immune skin and systemic responses to compounds including chemicals, cosmetics and pharmaceuticals with development of novel IP.
Anne is a Health Professional Clinical Scientist with experience in the regulatory framework involved in the development of ATMPs and is a partner in the Northern Alliance Advanced Therapy Treatment Centre.