Progress on a Community-Based Participatory Action Study About Pharmacogenes in the Minnesota Hmong Community

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OBJECTIVE

1. Determine allele frequencies of genetic variations of **Very Important Pharmacogenes** in the **Hmong community**
2. Identify key medicines that may require specific clinical guidance in Hmong people
3. Describe people's perceptions about these results

BACKGROUND

Precision Medicine

- **Pharmacogenomic** advances make it possible for clinicians to tailor how they prescribe medications to individual patients.
- **Very Important Pharmacogenes (VIPs)** are molecular targets that are known to be associated with drug response. Knowledge of an individual's genotype for VIPs can improve drug and dose selection.
- **Precision Medicine (PM)** could decrease health disparities in underserved populations by improving effectiveness, decreasing adverse effects, and possibly increasing medication compliance.
- **The Clinical Pharmacogenetic Implementation Consortium (CPIC)** has evidence-based guidelines about how genetic test results should be used to optimize individual medications.
- Clinicians could benefit from knowledge about allele frequencies in all of people, including rarely studied minority populations, such as the Hmong community.

Community-Based Participatory Action Research (CBPAR)

- The Hmong community is not adequately represented in many research studies
- In 2016, we used a CBPAR approach to identify cultural and ethical issues that could encourage Hmong people to participate in genomics research (Culhane-Pera et al 2016) and to successfully enroll 237 Hmong adults in a genomics study (Straka et al 2016).
- **The Hmong Genomics Research Board** (with 8 Hmong community members and 2 non-Hmong professionals) conducted 5 key informant interviews and 5 focus groups with 42 adults to identify barriers, facilitators, and potential processes for genomics project. We subsequently successfully collected genomic samples from 236 Hmong adults.
- CBPAR was effective because it **engaged the community** and **partnered community members with academicians** to ensure that the study was culturally and linguistically appropriate, addressed community concerns, and strengthened the credibility of the academic researchers.

AN EXAMPLE WITH COUMADIN

CYP2C9*3 (rs1057910)	Hmong No. Allele Copies	Hmong Allele Frequency	Han Chinese + Japanese No. Allele Copies	Han Chinese + Japanese Allele Frequency	P
Major A	372	0.802	173	0.961	
Minor C	92	0.198	7	0.039	<0.0001
Total (n)	464 (232)	1	180 (90)	1	

Table 1: SNP frequencies of *CYP2C9*3* in Hmong (N=236) were more prevalent (0.198 vs 0.039, p<0.0001) than in the reference population of combined Han Chinese and Japanese. This means Hmong people are more sensitive to the anticoagulation effect of coumadin.

METHODS

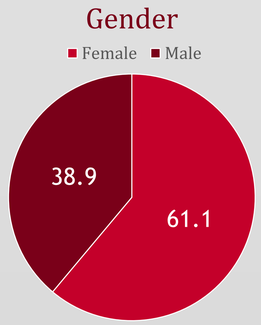
- **The Hmong Genomics Board** consists of
  - 8 academicians (4 UMN researchers, 4 students)
  - 3 community professionals (2 family physicians, 1 community researcher)
  - 6 community advisory members
- We created research design, linguistically-appropriate consent materials, and enrollment plan at 6 community locations (3 college campuses, a Hmong conference, a community clinic, and a Hmong senior center).
- We enrolled 198 Hmong adults, after obtaining consent in Hmong or English, completing demographic information, measuring height and weight, and collecting saliva samples.

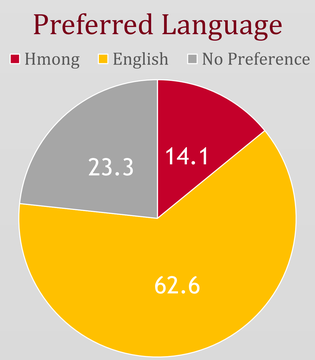
Tested Very Important Pharmacogenes and Medications - *Results pending*

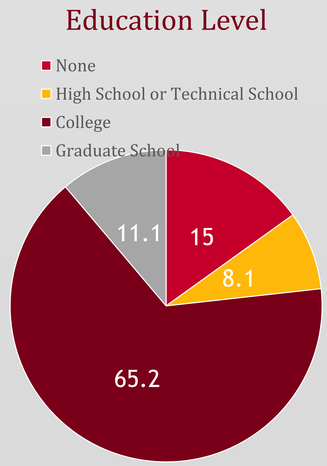
CYP2C19	Citalopram	CYP2D6	Codeine	CYP2D6, CYP2C19	Imipramine	SLCO1B1	Simvastatin
CYP2C19	Clopidogrel	CYP2D6	Desipramine	CYP2D6, CYP2C19	Trimipramine	TMPT	Azathioprine
CYP2C19	Escitalopram	CYP2D6	Doxepin	CYP3A5	Tacrolimus	TMPT	Mercaptopurine
CYP2C19	Sertraline	CYP2D6	Fluvoxamine	DPYD	Capecitabine	TPMT	Thioguanine
CYP2C19	Voriconazole	CYP2D6	Nortriptyline	DPYD	Fluorouracil	UGT1A1	Atazanavir
CYP2C19, CYP2D6	Amitriptyline	CYP2D6	Ondansetron	DPYD	Tegafur		
CYP2C9, VKORC1, CYP4F2	Warfarin	CYP2D6	Paroxetine	G6PD	Dapsone		
CYP2C9	Phenytoin	CYP2D6, CYP2C19	Clomipramine	G6PD	Rasburicase		

DEMOGRAPHIC RESULTS

- We enrolled 198 Hmong adults - ages 18-94 (32.5 ± 19.1) years







DISCUSSION

How participants and the Hmong community will respond to the results is not yet known. Hmong Genomics Board members identified:

- **possible positive responses:** increased trust and medication adherence due to increased efficacy and decreased side-effects after appropriate dose adjustment
- **possible negative response:** decreased trust in prescriptions for other medications that are not on the VIP pharmacogene list
- Focus groups with participants will help understand community response

How clinicians will respond to these results is not yet known. As precision medicine is a new field, CPIC guidelines for medication optimization only cover 35 gene and drug pairs. Insurance companies are also not yet paying for these tests.

- VIP-Hmong study results may serve as general suggestions for clinicians as they prescribe medicines for Hmong individuals
- It will be up to the discretion of individual providers to choose how and if they adjust the prescribed dosage of the studied medications for their Hmong patients
- Future discussions with clinicians could help understand their responses

CONCLUSION

- Using a CBPAR approach, the Hmong Genomics Research Board successfully enrolled 198 Hmong adults from a variety of genders, ages, education levels, and language preferences.
- The majority of participants were willing to be contacted about joining focus groups, joining other research studies and allowing their de-identified DNA samples to be used for future studies, which indicates their comfort with participating in genomics research.
- Genotyping data analysis is currently ongoing. From our previous pilot study on coumadin, we observed a significant difference in prevalence of the *CYP2C9*3* in the Hmong compared to the Han Chinese and Japanese. There may be differences in prevalence amongst the SNPs in this study.

REFERENCES

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