

## POPH20001 Genetics Health & Society Notes

- **Prevention of Severe Skin Reactions by HLA-B\*15:02 Testing**

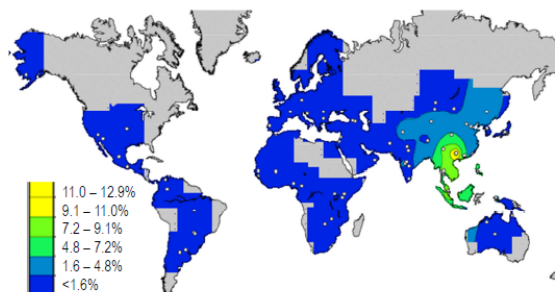
- Found to be most prominent of Southern China

### Carbamazepine-SJS

Association with HLA-B\*15:02 in Asians

Population	HLA-B*1502 +ve/-ve (n)		Odds ratio
	CBZ-SJS	CBZ-tolerant	
Chinese (Taiwan) <sup>1</sup>	44/0	3/98	2,504
Chinese (Hong Kong) <sup>2</sup>	24/2	16/119	89
Chinese (mid China) <sup>3</sup>	8/0	4/45	184
Chinese (south China) <sup>4</sup>	13/5	12/81	17.6
Thai <sup>5</sup>	6/0	8/34	25.5
Thai <sup>6</sup>	37/5	5/37	54.8
Hindu Indian <sup>7</sup>	6/2	0/10	71.4
Malay <sup>8</sup>	4/0	0/6	117

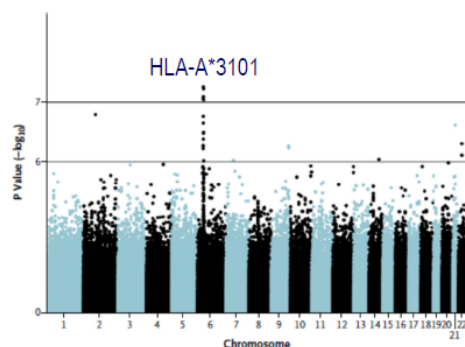
Ethnic Distribution of HLA-B\*15:02



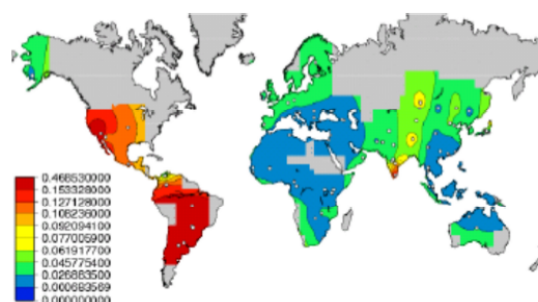
- 4,877 subjects indicated for carbamazepine enrolled
- HLA-B\*15:02 genotyped in 4,855
- 447 (7.7%) positive: Carbamazepine avoided
- 2,283 (2.3%) negative: 4,120 give carbamazepine
- 211 (4.3%) developed mild skin rashes
- No case of Stevens Jonson syndrome (historical estimate 10 cases;  $p < 0.001$ )
- Practice adopted in Hong Kong, Taiwan, Thailand, Singapore
- This has led to study led to a change in policy by the FDA to screen for the allele HLA-B\*15:02 before giving carbamazepine as treatment

- **HLA-A\*31:01 and Genome-Wide Association**

- Through the genome-wide association study, HLA-A\*31:01 allele was found to be a genetic risk factor for carbamazepine-hypersensitivity in Japanese and European population



HLA-A\*3101



- **Lesson from Carbamazepine-HLA-b\*15:02 Case**

- Presence of genetic variants of very large pharmacological effect size (odds ratio  $> 1000$ )
- Associations can be ethnic specific, drug specific and phenotype specific
- Population based pharmacogenetics screening can be effective