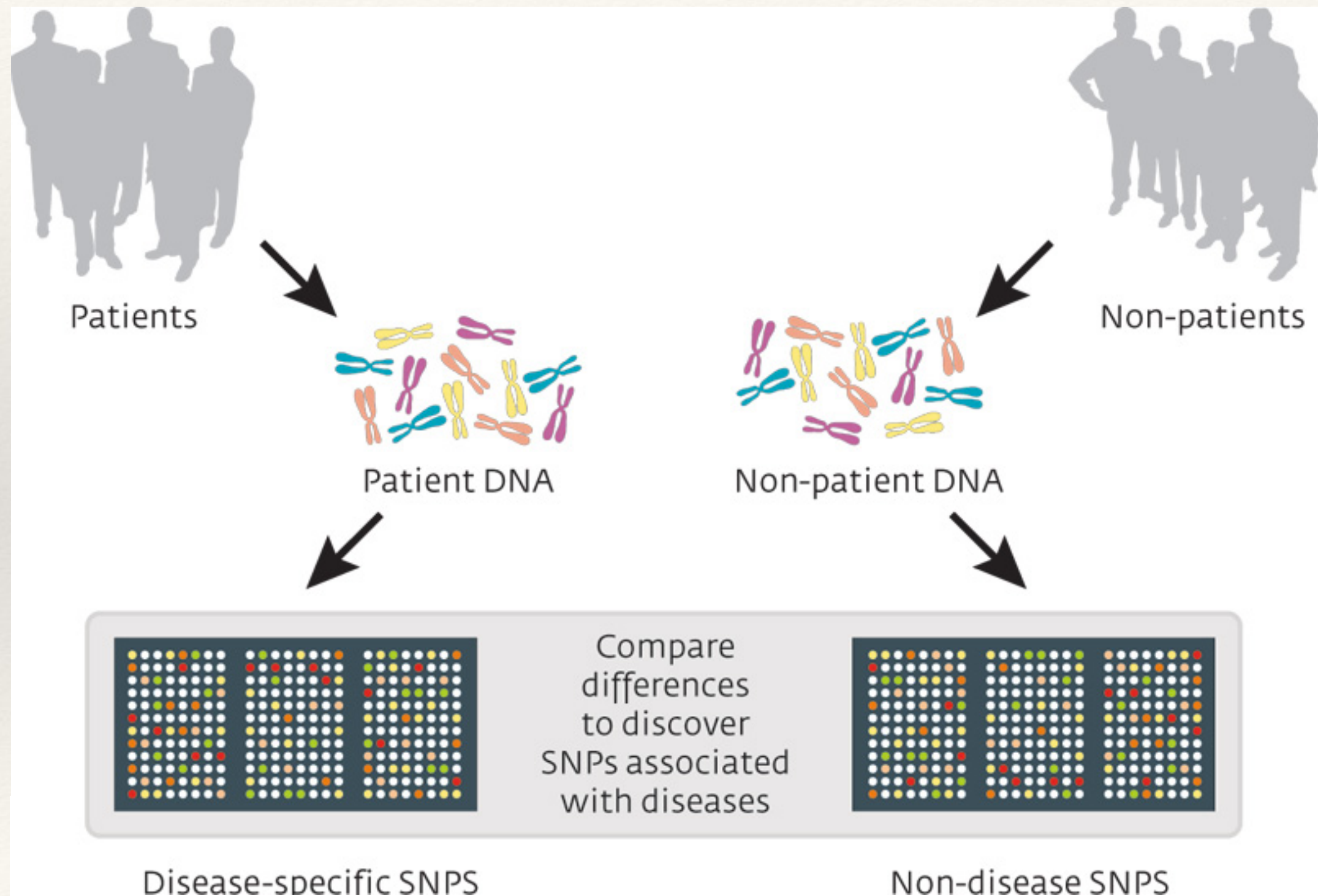


# Borrowing from human genetics: Genome-wide Association studies (GWAS)



# Sequence kernel association test (SKAT)

- ❖ Whole-genome sequencing can detect rare variants
- ❖ Group variants into genes and testing for association
- ❖ Variants can be assigned weights:  $f(G_i)$
- ❖ Can easily obtain a p-value for each gene

**Linear model:**

The diagram shows the linear model equation  $y_i = \alpha_0 + \alpha' \mathbf{X}_i + \beta' \mathbf{G}_i + \varepsilon_i$ . Above the equation, three labels are positioned: 'disease/ phenotype' above  $y_i$ , 'covariants (e.g. age, sex)' above  $\alpha' \mathbf{X}_i$ , and 'variant sets (e.g. genes)' above  $\beta' \mathbf{G}_i$ . Arrows point from each label to its corresponding term in the equation: a vertical arrow from 'disease/ phenotype' to  $y_i$ , a vertical arrow from 'covariants' to  $\alpha' \mathbf{X}_i$ , and a diagonal arrow from 'variant sets' to  $\beta' \mathbf{G}_i$ .

$$y_i = \alpha_0 + \alpha' \mathbf{X}_i + \beta' \mathbf{G}_i + \varepsilon_i$$

**null model:**

$$y_i = \alpha_0 + \alpha_1' \mathbf{X}_i + \varepsilon_i$$

Wu et al., *Am. J. Hum. Genet.*, 2011