

Benefits of Constructing a DNA Bank to Support Multi-Center Clinical Trials

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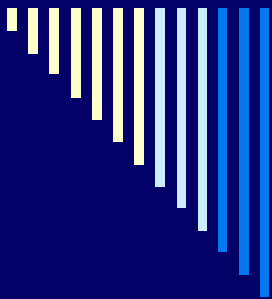


A DNA Bank Would Aid Clinical Trials

- Ability to measure & adjust for ethnic stratification
 - Potential for increased statistical power
 - Identification of high-risk patients
 - Identification patients likely to benefit for therapy
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Measurement of Ethnic Stratification

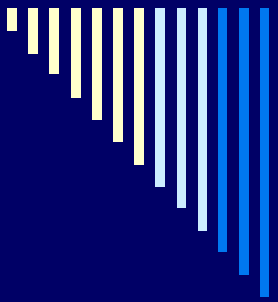




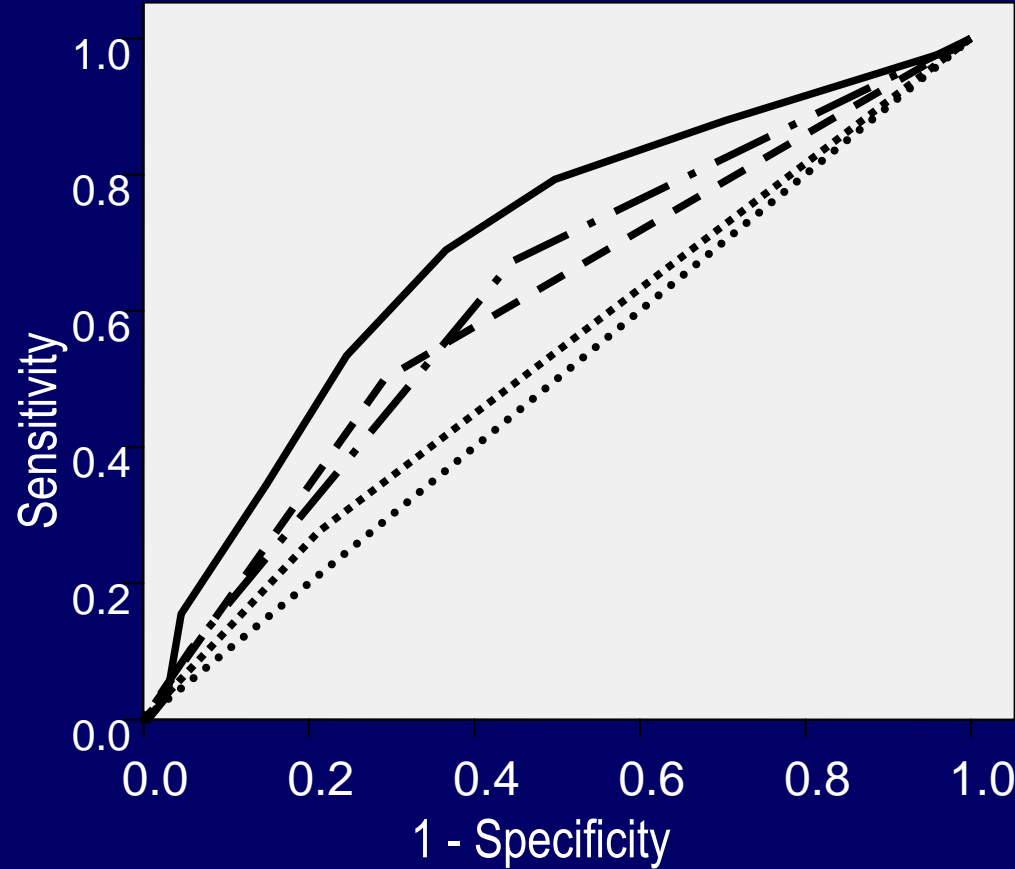
Identification of At-Risk Patients

- IL-6 -174 [rs1800795]
- TNF- α -308 [rs1800629]
- TLR4 +896 [rs4986790]
- CD14 -159 [rs2569190]
- IL-1 β -31 [rs1143627]

- Fishman et al. 1998. *J Clin Invest* 102:1369-1376. IL-6 Juvenile arthritis
- Mira et al. 1999. *JAMA* 282:561-568. TNF- α Severe sepsis
- Arbour et al. 2000. *Nat Genet* 25:187-191. TLR4 LPS response
- LeVan et al. 2001. *J Immunol* 167:5838-5844. CD14 Transcription
- Wang et al. 2003. *Hepatology* 37:65-71. IL-1 β Hepatocarcinoma



Identification of At-Risk Patients



Source of the Curve

- Reference Line
- Age ≥ 50
- - - 3rd Degree Burn Size $\geq 30\%$
- . - Age ≥ 50 + Burns $\geq 30\%$
- Age ≥ 50 + Burns $\geq 30\%$ + Genes

Barber et al. 2007 JBCR 28: 205-11.



Identification of At-Risk Patients

Variable	Area	95% CI		Added Area
		Lower	Upper	
Age \geq 50	.532	.445	.619	--
3 rd Degree Burns \geq 30%	.604	.518	.690	.072
Age \geq 50 + Burns \geq 30%	.617	.534	.700	.013
Age \geq 50 + Burns \geq 30%+ Genes	.691	.612	.770	.074



Genetics Can Aid Post-Hoc Analysis

- Specific pathway containing a polymorphic gene
 - eg: TNF- α SNP and anti-TNF therapy
 - Build individual likelihood of benefit into analysis
 - Analysis of a candidate SNPs costs ~\$2K
 - Particularly useful if trial fails
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Relatively Cheap and Easy

- Only one sample per patient is needed
 - Extraction cost is low ~\$10.00 per sample
 - DNA can be extracted from many tissues
 - DNA is stable - analysis need not be immediate
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