Personalized Medicine

- We are all different..
- This is why personalized medicine is important to everyone.

- Why does someone need twice the standard dose to be effective?
- Why does this drug work for you but not me?
- Why do I have side-effects and you don't?
- Why do some people get cancer and others dont

Is Medicine a Science or an Art?

If it were not for the great variability among individuals, medicine might well be a science, not an art.

- Sir William Osler, Physician 1892
- Father of modern medicine

The Goal of Personalized Medicine

- The Right Dose of
- The Right Drug for
- The Right Indication for
- The Right Patient at
- The Right Time.

Pharmacogenetics & Pharmacogenomics

- **Pharmacogenetics is the study of the genetic basis for variation in drug response.**

- Pharmacogenetics: The role of genetics in drug responses.
  - F. Vogel. 1959
- **Pharmacogenomics: The science that allows us to predict a response to drugs based on an individuals genetic makeup**
  - Felix Frueh, Associate Director of Genomics, FDA
- Pharmacogenomics →
  - employs tools for surveying the entire genome &
  - Assess multigenic determinants of drug response.

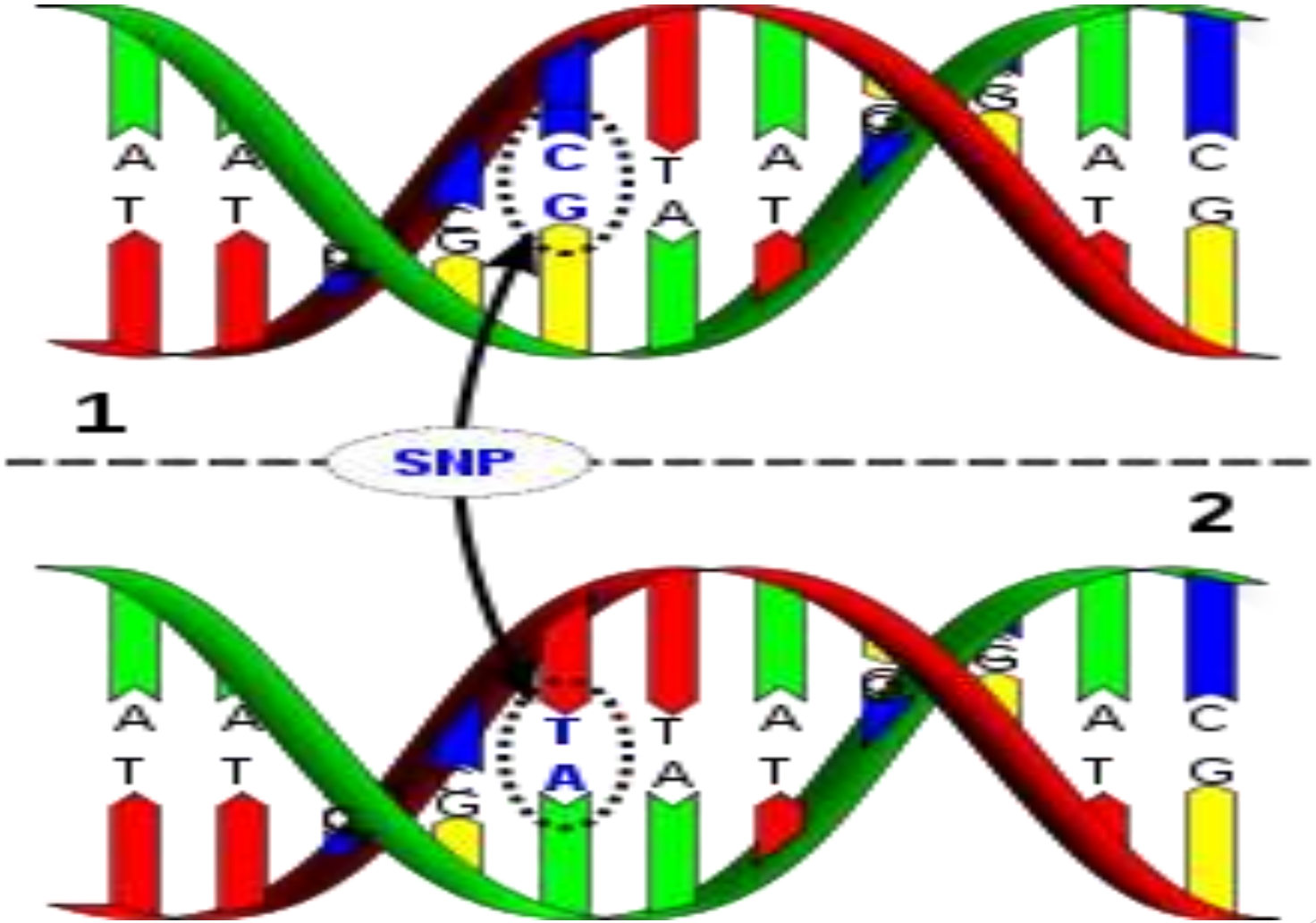
Pharmacogenetics

- Due to genetic polymorphism
- Types of genetic polymorphism
  - Single nucleotide polymorphism (SNP) → more common, less serious
  - Insertion/ deletions (indels) → less common, serious

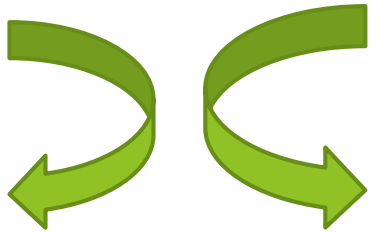
Examples of Genetic Polymorphisms Influencing Drug Response

GENE PRODUCT *(GENE)*	DRUGS	RESPONSES AFFECTED
		Drug Metabolism and Transport
CYP2C9	Tolbutamide, warfarin, phenytoin, nonsteroidal anti-inflammatory	Anticoagulant effect of warfarin
CYP2C19	Mephenytoin, omeprazole, voriconazole	Peptic ulcer response to omeprazole; cardiovascular
	hexobarbital, mephobarbital, propranolol,	events after clopidogrel
	proguanil, phenytoin, clopidogrel	
CYP2D6	®blockers, antidepressants, anti-psychotics,	Tardive dyskinesia from antipsychotics, narcotic
	codeine, debrisoquine, atomoxetine	side effects, codeine efficacy, imipramine dose
	dextromethorphan, encainide, flecainide,	requirement, ®blocker effect; breast cancer
	fluoxetine, guanoxan, *N*-propylajmaline,	recurrence after tamoxifen
	perhexiline, phenacetin, phenformin,	
	propafenone, sparteine, tamoxifen	
CYP3A4/3A5/3A7	Macrolides, cyclosporine, tacrolimus,	Efficacy of immunosuppressive effects of
	Ca^{2+} channel blockers, midazolam, tacrolimus	
	terfenadine, lidocaine, dapsone, quinidine,	
	triazolam, etoposide, teniposide, lovastatin,	
	alfentanil, tamoxifen, steroids	

Single Nucleotide Polymorphism(SNP)



Consequences of polymorphism



Pharmacokinetic Variations

(involving drug metabolism)

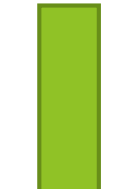
Phase I Phase II

Pharmacodynamic Variations

(involving drug-receptor interactions)

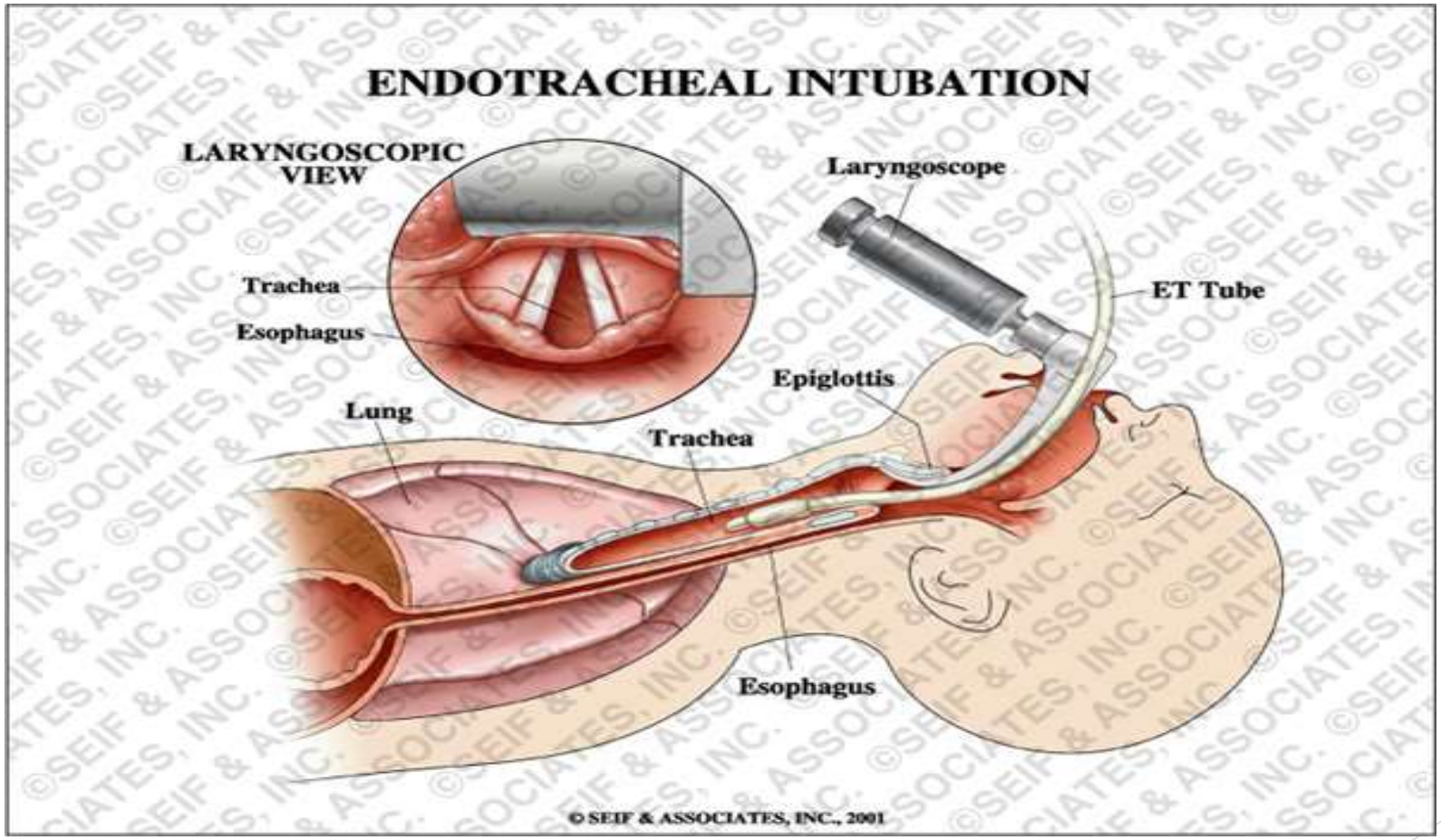
Pharmacokinetic Variations

Succinyl choline



Atypical Psuedocholinesterase

Pharmacokinetic Variations



Pharmacokinetic Variations

Isoniazid

N Acetyl transferase

Fast Acetylators

Slow Acetylators

Pharmacokinetic Variations

Acetylation

Polymorphism of N-acetyl transferase

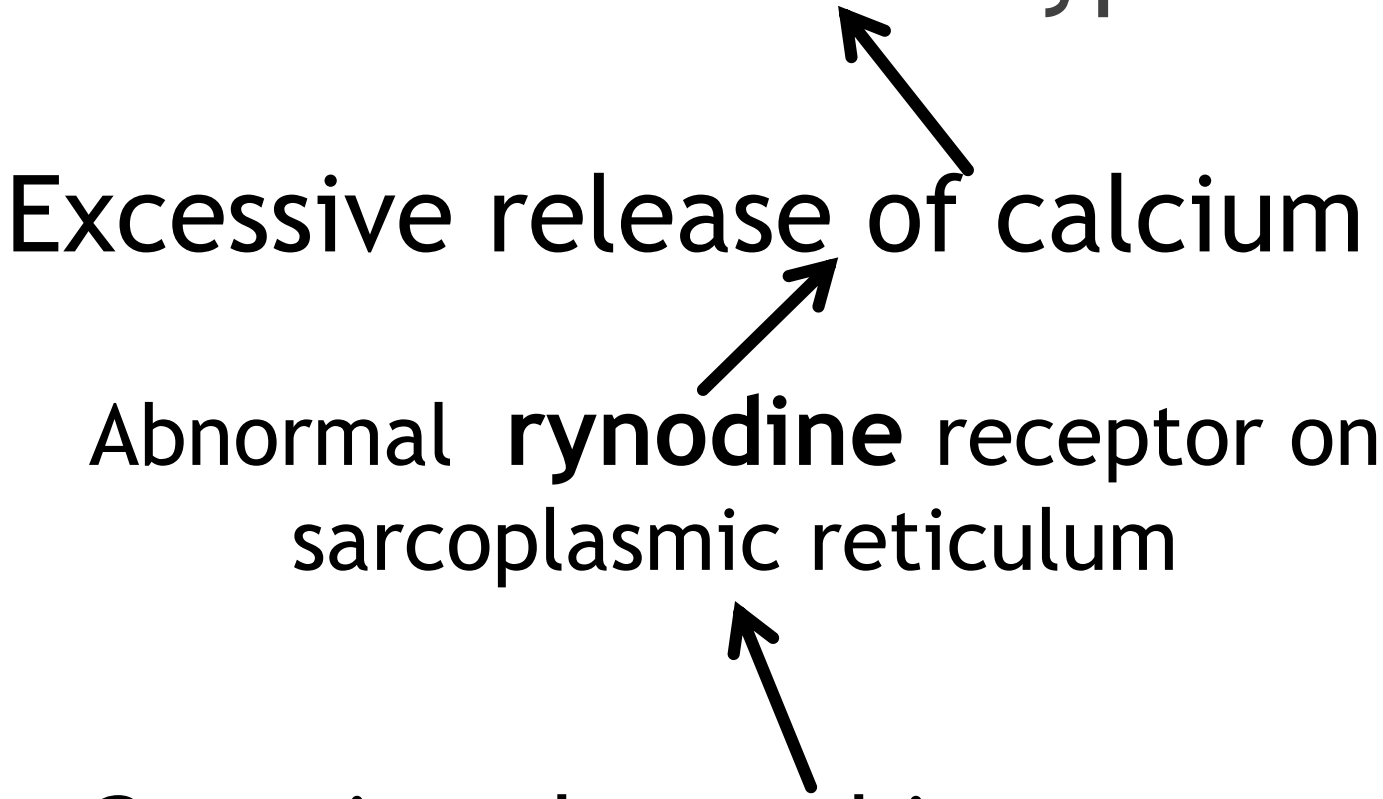
Acetylation of Isoniazid

Fast acetylators
hepatotoxicity

slow acetylators
peripheral neuropathy

Pharmacodynamic variations

- Halothane induced hyperthermia



Other examples

- Precipitation of PORPHYRIA by barbiturates
- Haemolysis due to G6PD deficiency.
- Insulin resistance due to receptor mutations

IDIOSYNCRACY

- Genetically mediated abnormal reactivity to a chemical in a small minority of individuals for which no definite genotype has been described.
- Cause unknown.
- Not found in majority of population.
- Aplastic aneamia due to chloramphenicol

Applications of pharmaco genetic knowledge

- Personalise medicine
  1. To enhance effectiveness
  2. Decrease ADR
  3. To make clinical trials faster & cost effective

LIMITATIONS

- **Expensive and time consuming.**
- Influence of **environmental factors**
- **Ethical issues**