ABC’s of Research: Role of Serendipity, Perseverance, and Risk

Katrina Mealey, DVM, PhD
DACVIM, DACVCP
ABC Drug Transporters
P-glycoprotein
Serendipity (A)  
$abcb1^{-/-}$ knockout mouse  

- Schinkel Laboratory NCI Netherlands  

Mycopites musculinus
IVERMECTIN:
“White feet—don’t treat!”
Perseverance (B)

- Finish PhD-get real job
  - Not get ‘scooped’

- Obtain DNA from ‘ivermectin sensitive’ dogs
  - $$

- Find a laboratory to do the research
  - Benchtop in a lab in a different department

- Find time to do research
  - Clinics/teaching
Canine ABCB1 Polymorphism

275 TGGTTTTTGGAACATGACAGATAGCTTTGCAAATGCAGGAATTTCAAGAAACAAAACTTTT

337 CCAGTTATAATTAATGAAAGTATTACGAACAATACACAACATTTCATCAACCATCTGGAGGA

399 GGAAATGACACGTATGCTATTATTACAGTGGGATCGGTGCTGGCGTGCTGGTGGCTGCTT

461 ACATCCAGGTTTTCCATTCTGTTGCCTGGCAGCAGGAAGACAGATACTCAAAATTAGAAAACAA

523 TTTTTTCTCATGCTATCATGCGACAGGAGATTGGCTGGTTTGACGTGCATGACGTTGGGGAGCT

585 TAAACCCCGGCTCACAGACGATGTCTCCAAAATCAATGAAGGAATTGGCGACAAAGTTGGAA

647 TGTTCTTTTCAATCAATACCAACATTTTTTCACCACGGTTTTTATAGTGTTGGGGGTTTACACGTGTT

708 TGGTTTTTCAATCAATACCAACATTTTTTCACCACGGTTTTTATAGTGTTGGGGGTTTACACGTGTT
P-glycoprotein
ABCB1 gene

= ATP binding sites
= Substrate binding sites
P-glycoprotein (Mutation)
ABCB1 (wt/wt) pre-treatment
ABCБ1 (wt/wt) 0.2 mg/kg loperamide (Imodium) – 4 hours post treatment
ABCB1 (mut/mut) pre treatment
ABCB1 (mut/mut)  Loperamide (Imodium)  
4 hours post treatment
ABCB1 (mut/mut) Loperamide (Imodium) 4 hours post treatment; Naloxone
Land grant mission—bring discoveries to the public

- Pharmacogenetic Testing
  - No interest in licensing MDR1 test
    - IDEXX
    - Antech
  - “Not a market...”
  - “Not profitable”
Preventable Ivermectin Toxicity

22 October
10 November
Risk (C)

- Licensed the patent from WSU

- WSU Service Center
  - 50,000+ dogs tested in U.S.
  - Licensed on 3 continents
  - And Mars!

- Patent generated funding for WSU
  - Service Center → $3,000,000
  - >$750,000 in royalties/licensing fees to Office of Commercialization

- ..to cover patent costs for YOUR discoveries
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