Patient Story 6: (Kelly Ranallo)

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- My daughter, Allie, was diagnosed at the age of 8 with mosaic Turner Syndrome (TS) - 45XO 46XX - approximately 80% normal cells and 20% TS cells.

- Her first medication complication was noted following a foot surgery for Bilateral Brachimetarsia. She experienced poor recovery from anesthesia with extreme nausea and hallucinations. She also experienced poor pain management with use of Oxycodone and Oxycontin.

- Despite continued reports that her pain was better controlled with Tylenol and or Advil the nursing staff and physicians kept telling her it wasn't possible and she just had a low pain tolerance and implied drug seeking behaviors.

Patient Story 6 (Cont.): Drug Side Effects

- During this same period, she was started on hormone replacement for suspected premature ovarian failure related to the TS diagnosis. After the initiation of Estrogen she has extreme complication of prolonged heavy bleeding and therefore was started on Progesterone to help regulate her cycles.

- While on the Progesterone she reported significant dizziness and feeling as if she was going to pass out, often requiring her to come home from school on a daily basis.

- When this was reported to her provider the response was "*have her take it at night that way she will sleep through the side effects and it won't impact her school schedule*".

Patient Story 6 (Cont.): Genetic Testing

- Not content with that solution we self-referred to a Personalized Medicine clinic to undergo genetic testing to assess her drug metabolism. The molecular genetics results reported findings for two genes (called CYP2C19 and CYP2D6), involved in regulating drug metabolism.

- The following is a more technical description of this genetic finding:
  - *2*2 genotype on the CYP2C19 resulting in a poor metabolizer of this drug pathway (Progesterone included) and
  - *1/*2A genotype on the CYP2D6 which is associated with a ultra rapid metabolizer (Oxydontin included)

Patient Story 6 (Cont.): Impact of the Genetic Testing

- We were glad that her genetic finding confirmed her symptomatic reporting.
- Although the information is not 100% predictable for all drug metabolism, it did empower us to help her make better decisions on what drugs might be toxic to her as well as which one provided her a better outcome when she needed pain management for future surgeries.
- YouTube link: Hope, A Parents Perspective (Interview with Kelly Ranallo): https://www.youtube.com/watch?v=axCmVaWrolY

Example:
How Genetic Testing Was Helpful in Managing Allie's Care?

- Most recently she was started on anti-anxiety medication (Lexapro). When the first increase in dosing had significant side effects, we produced her drug metabolism report to demonstrate the prescribed drug was classified as a poor metabolized drug for her. This report included a series of tables showing which drugs are being metabolized by these two genes (see examples in the next slides).

- As a result, her provider made an immediate change in the dosing that typically they would not make for a 4-6 week "adjustment" period and she stabilized on the drug in under a week.

- This genetic information has and continues to impact the outcome of Allie prescription drug management. It may not be perfected, but it has definitely impacted the overall outcome of her health and medical management.

Example: Genetic Testing Report Drugs Metabolized by CYP2C19

Here is an example of a genetic testing report for drug metabolism genes. The below table and description were included in the patient report.

Table for Drugs and CYP2C19 Metabolism*		
Proton Pump Inhibitors	Anti-depressants	
esomeprozole (Nexium®), lansoprazole (Prevacid®), omeprazole (Prilosec®), pantoprazole (Protonix®), rabeprazole (Aciphex®)	amitriptyline (Elavil®), citalopram (Celexa®), clomipramine (Anafranil®), escitalopram (Lexapro®), imipramine (Tofranil®), sertraline (Zoloft®)	
Anti-epileptics	Oncology	
diazepam (Valium®), mephobarbital (Mebaral®), phenobarbital (Luminal®), phenytoin (Dilantin®), primidone (Mysoline®)	cyclophosphamide (Cytoxan®), nilutamide (Nilandron®), teniposide (Vumon®), thalidomide (Thalomid®)	
Hormone	Blood Pressure	
progesterone (Endometrin®)	propranolol (Inderal®)	
Pain Treatment	Anti-infective	
carisoprodol (Soma®), indomethacin (Indocin®)	chloramphenicol (AK-Chlor®), proguanil (Malarone®)	
Anti-retroviral	Blood thinner/Anti-platelet	
nelfinavir (Viracept®)	Warfarin (Coumadin®)	Produg: clopidogril (Plavix®)

*This table contains examples of medications that can be affected by mutations in the CYP2C19 gene. Care should be taken with all medications and a conversation should occur between the patient and the provider to ensure up-to-date information is assessed prior to prescribing any medication.

Example: Genetic Testing Report Drugs Metabolized by CYP2C6

Here is an example of a genetic testing report for drug metabolism genes. The below table was included in the patient report.

Table for Drugs and CYP2D6 Metabolism*		
Antidepressants		Antipsychotics
amitriptyline (Elavil®), clomipramine (Anafranil®), desipramine (Norpramin®), duloxetine (Cymbalta®), fluoxetine (Prozac®), fluvoxamine (Luvox®), imipramine (Tofranil®), nortriptyline (Pamelor®), paroxetene (Paxil®), sertraline (Zoloft®), venlafaxine (Effexor®)		Haloperidol (Haldol®), perphenazine(Trilafon®), riseridone (Risperdal®), chlorpromazine (Thorazine®), thioridazine, zuclopenthixol, aripiprazole (Abilify®), thioridazine (Mellaril®)
Antihypertensives		Antiarrythmics
Diltiazem(Cartia®), carvedilol (Coreg®), metoprolol (Toprol®), propranolol (Inderal®)		Propafenone, encainide, flecainide (Tambocor®), lidocaine, mexiletine
Pain Treatment		Gastrointestinal
Oxycodone (Oxycontin®) Lidocaine (Lidoderm®)	Prodrugs: Codeine, Tramadol (Ultram®)	Metoclopramide (Reglan®), ondansetron (Zofran®), promethazine (Phenergan®),
Cough, Cold, Antihistamine		Oncology
Dextromethorphan, chlorpheniramine		Prodrug: Tamoxifen (Nolvadex®)
Other:		
Amphetamine, atomoxetine (Straterra®), timolol (Timoptic®)		