The Personalized Medicine Revolution

Diagnosing and Treating Disease Are About to Change Forever

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Why Do We Need Personalized Medicine?

- Many drugs don't work for or harm the patients they are prescribed for due to a "one size fits all" approach
  - Need to determine who will benefit and who will not, avoid "trial and error" therapy
- Currently disease is often detected too late, leads to high costs and poor outcomes
  - Need to detect and treat signs of disease before it becomes a problem, not after becoming ill

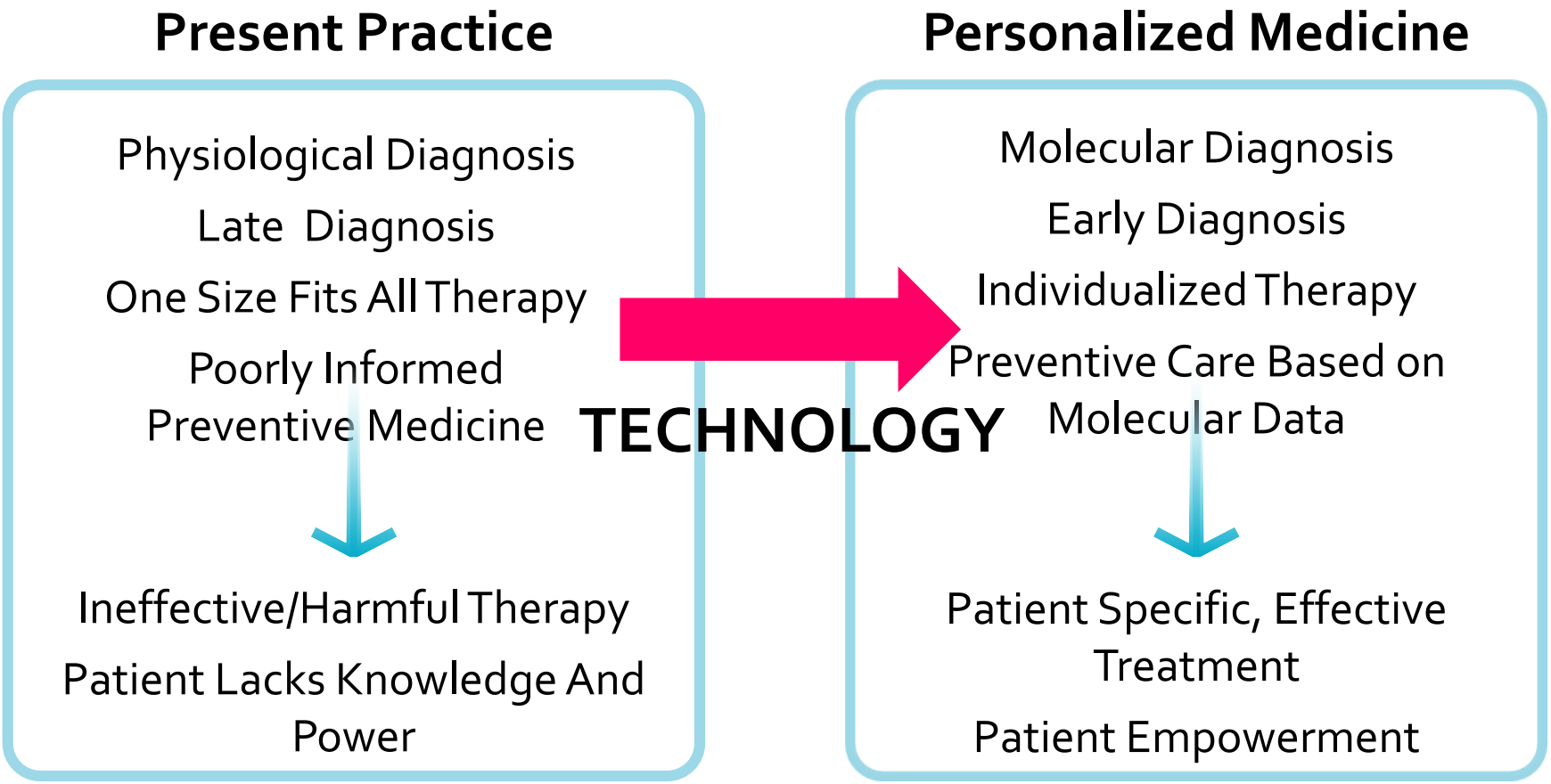
Current Medicine: "One Size Fits All" Healthcare

The problem is, we are all very different!

How Are We Different From Each Other?

1) Different genetic makeup
   - Up to three million differences in genetic makeup between you and anybody else (sex, ethnicity, physical appearance etc)
2) Different clinical background
   - Different ages, disease history, drug prescriptions
3) Different environmental factors
   - Different bacteria living in and on our bodies
   - Differences in lifestyle, nutrition, exercise, pollution, climate

Personalized Medicine: A Revolution In Medical Practice Enabled By Technology

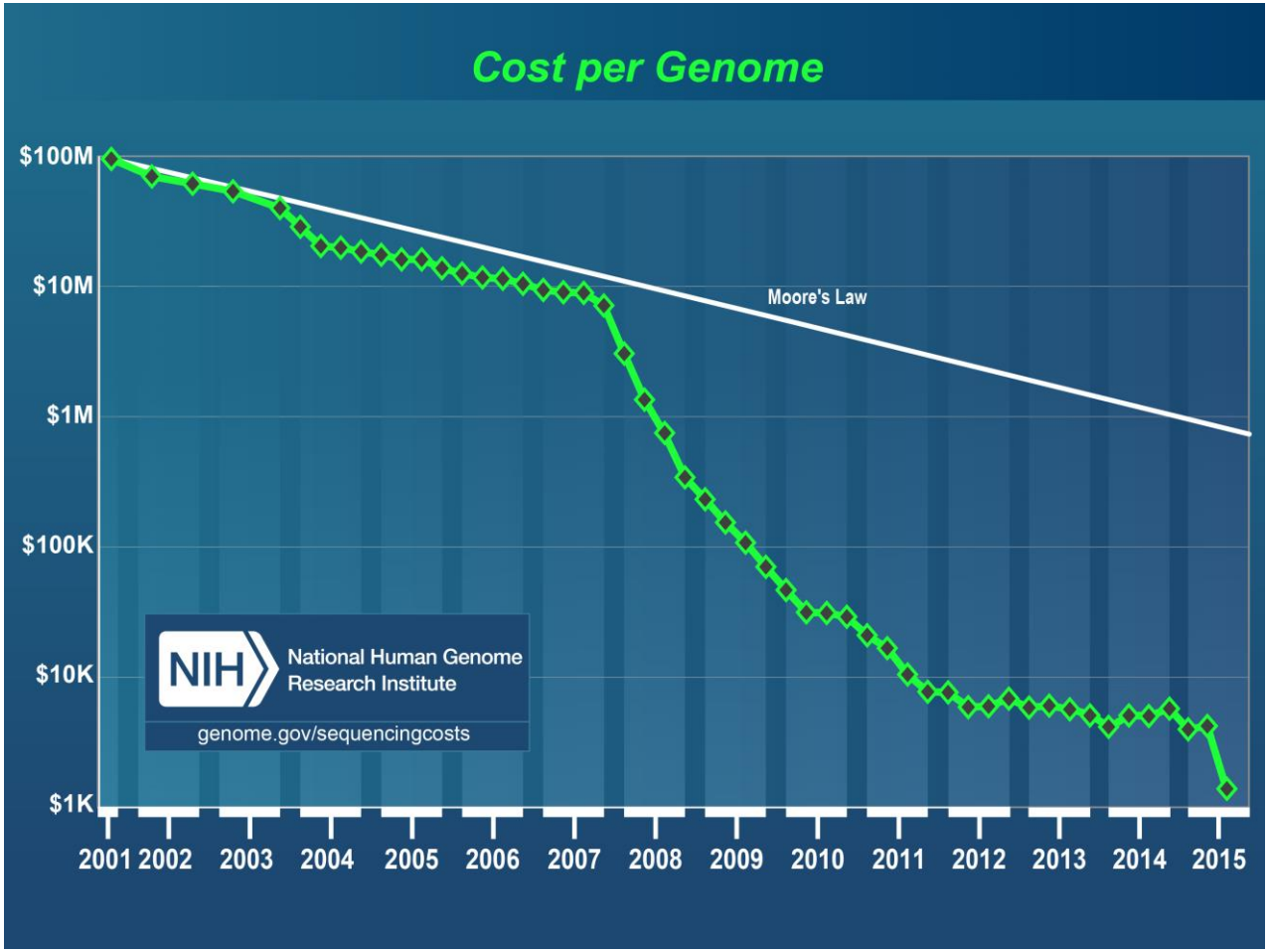


Forces Driving Personalized Medicine

1) Rapid technological change (inexpensive molecular level analyses, information technology)
2) Patient safety (adverse drug reactions)
3) Drug efficacy (50% of drugs don't work for individuals)
4) Consumer demand (individualized, effective, non-toxic treatment)
5) Preventive medicine (need individualized, definitive data)

A tsunami of change is about to hit the medical system

Technological Change: Costs of Personalized Molecular Measurements are Decreasing Dramatically



The cost of genome sequencing has decreased by nearly a million-fold since 2000

Patient Safety: Adverse Drug Reactions Are the Fourth Leading Cause of Death in North America

Cause of death	Number of deaths
Heart disease	743,460
Cancer	529,904
Stroke	150,108
Adverse drug reactions	106,000 (range 76,000-137,000)
Pulmonary disease	101,077
Accidents	90,523
Pneumonia	75,523
Diabetes	53,894

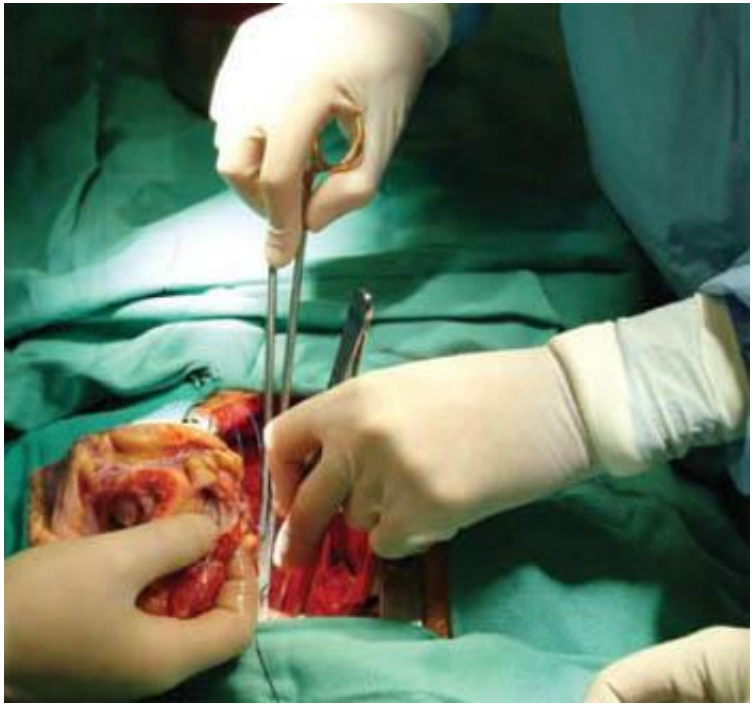
90% of adverse drug reactions are not reported

ADR Example: Doxorubicin-Induced Heart Toxicity

- Anticancer drug doxorubicin (used for 70% of childhood cancers, breast cancer patients, 1M patients/yr)
- 10-30% of patients suffer heart failure; increased severity in children
- May cause death, require heart transplant or reduced heart function that lasts a lifetime
- **Some people are much more susceptible than others due to their genetic makeup**

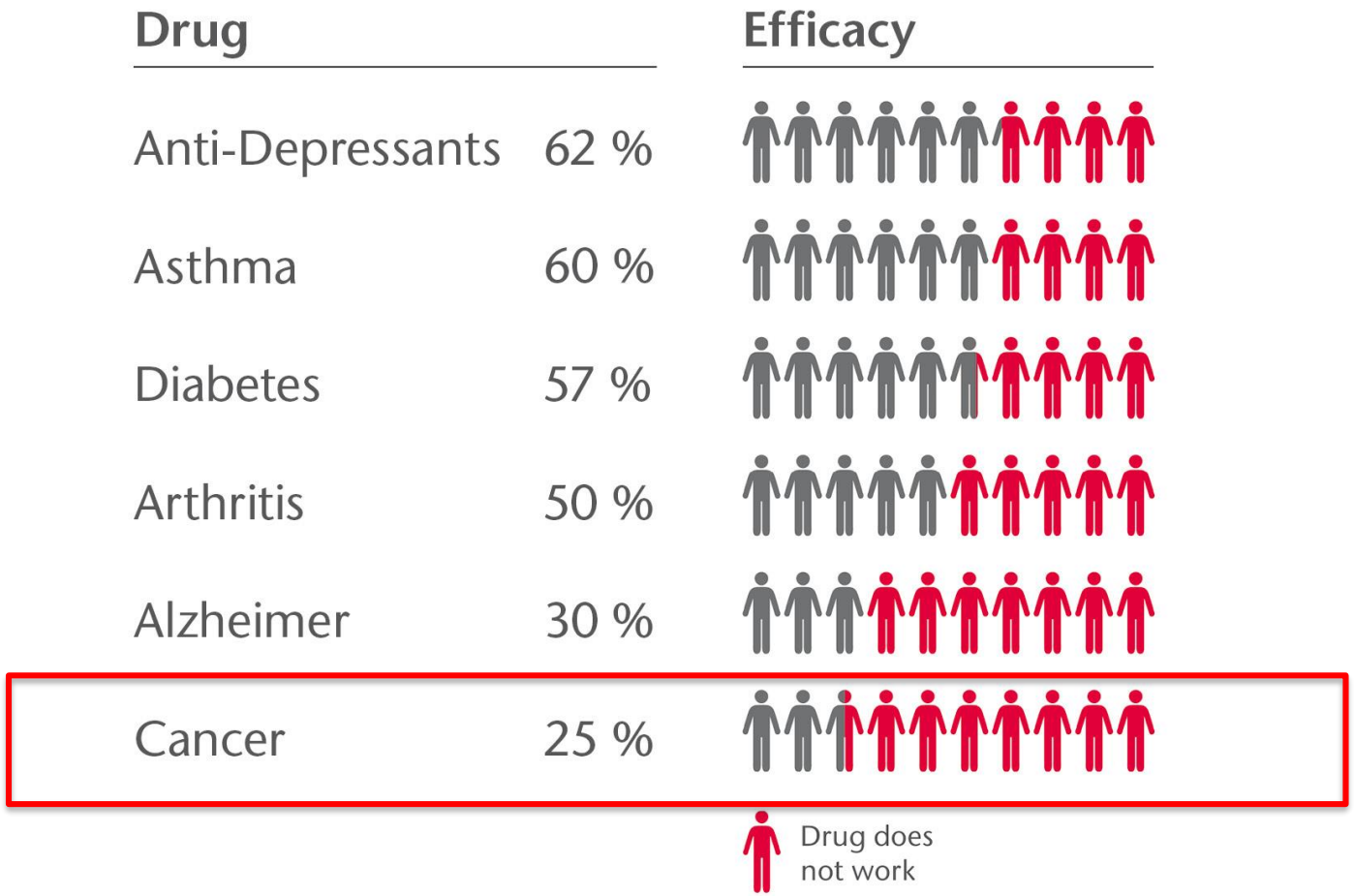
ADR Example: Doxorubicin-Induced Heart Toxicity

- 12 year-old boy presents with pain in abdomen
- Diagnosed with lymphoma
- Undergoes chemotherapy
- After second round of chemotherapy becomes breathless after walking a few steps
- Diagnosed with heart failure
- Requires heart transplant

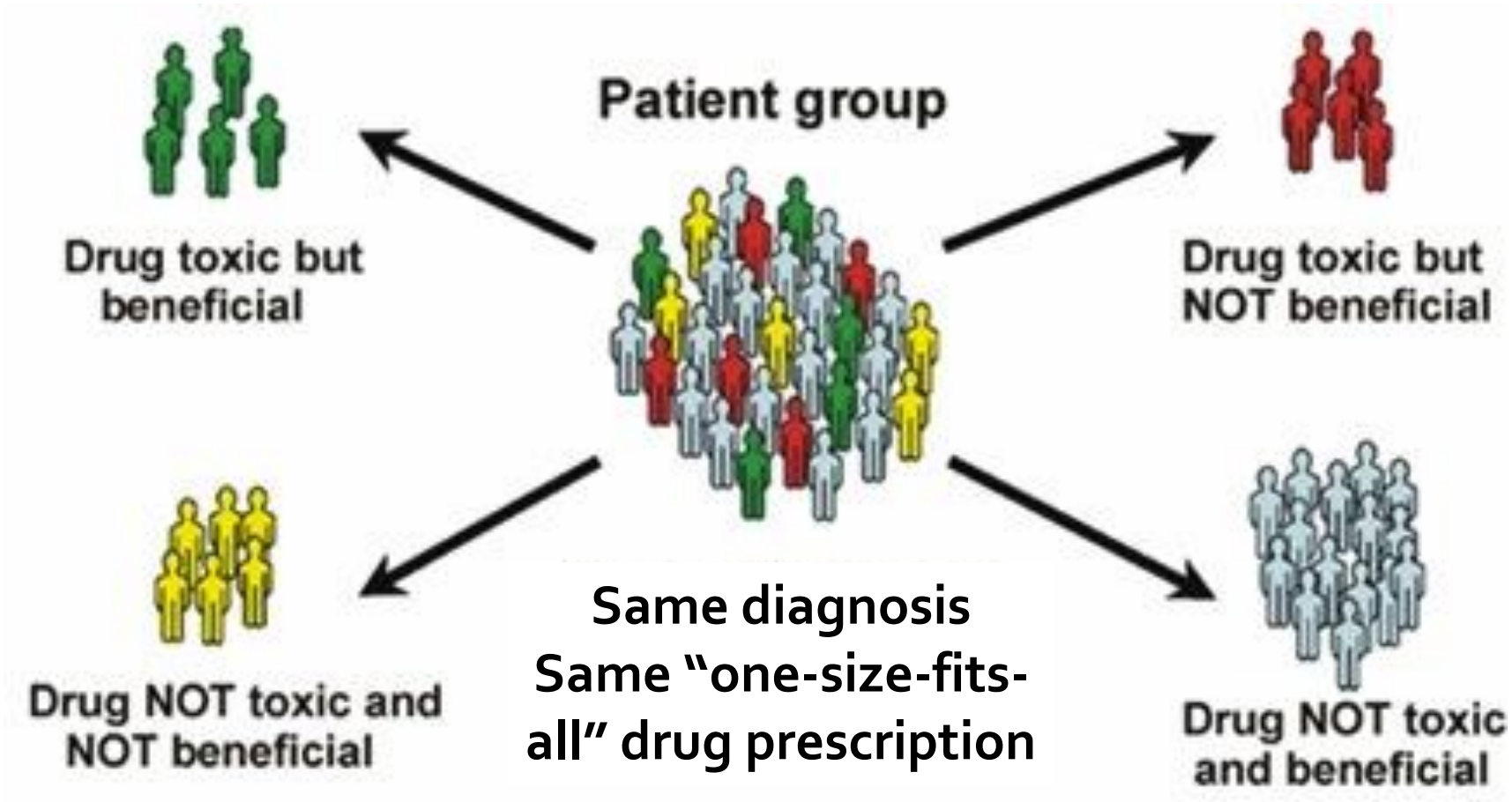


Heart Transplant

Drug Efficacy: Less Than 50% of Drugs Work on the Patient They are Prescribed For



How Can Personalized Medicine Help Prevent Adverse Dug Reactions and Ensure Efficacy?



Need to use molecular profiles to "stratify" patients so they receive the most appropriate therapy

Example: Genetic Tests To Guide Drug Prescription For Cancer Treatment

Problem:

- 75% of cancer drugs do not work on the person they are given to
- All cancer drugs can be very toxic

Solution:

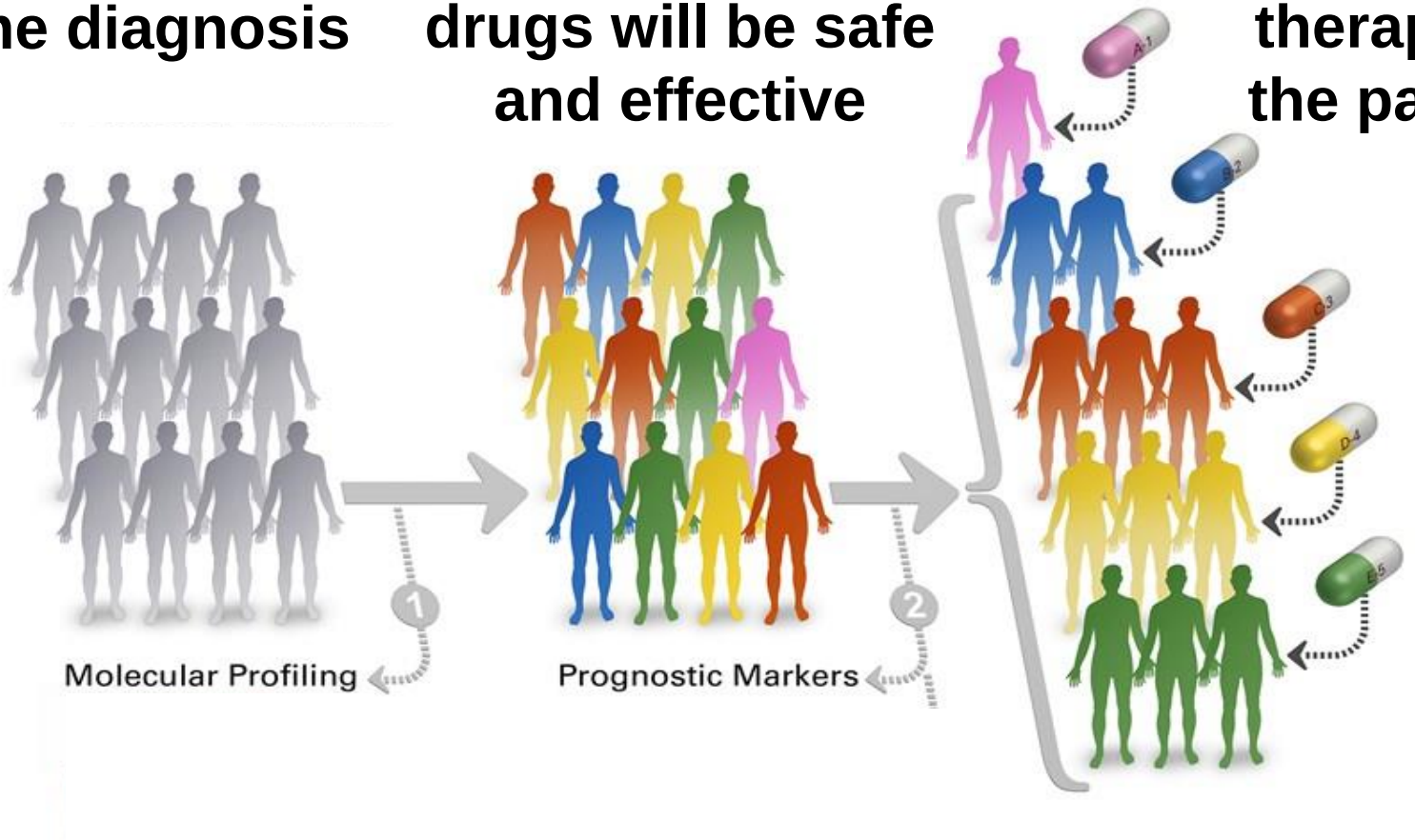
- Sequence the cancer genome to determine cancer-causing mutations
- Treat cancer with drugs that target the mutations
- Sequence the normal genome to determine potential for adverse drug reactions

Personalized Medicine: Genetic Tests To Guide Drug Prescription For Cancer Treatment

Same diagnosis

Test to see which drugs will be safe and effective

Match therapy to the patient



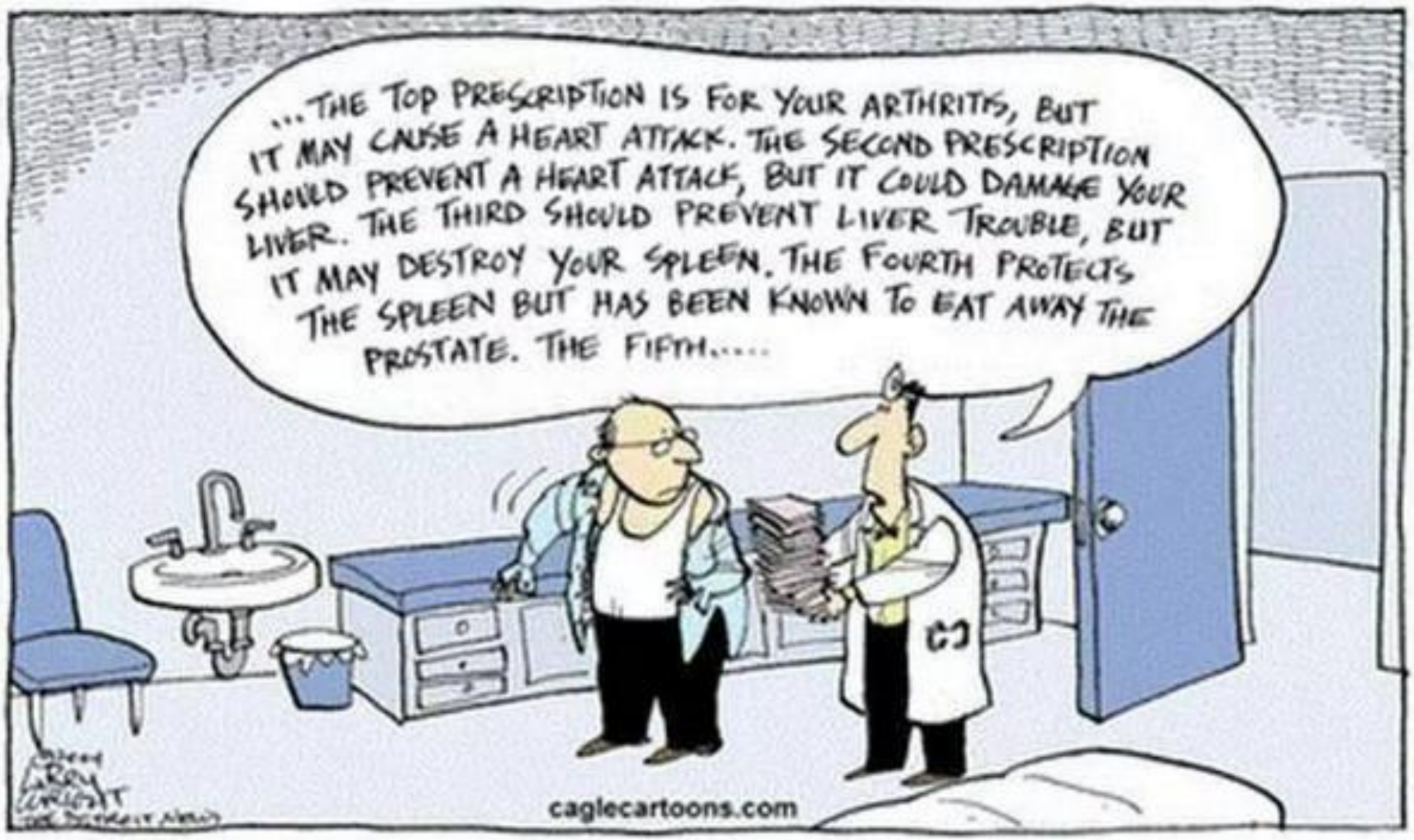
Personalized Medicine Can Revolutionize Cancer Treatment

- Trish Keating: diagnosed with colon cancer 6 years ago
- Multiple rounds of chemotherapy, relapsed each time
- Stage 4 cancer-disseminated throughout her body
- Cancer genome sequenced, cancer cells relied on a gene that could be inhibited by a blood pressure drug
- Six weeks after treatment cancer disappeared, still in remission 1 yr later

What About Drugs For Other Diseases?

The more drugs you take the greater the chance of an adverse drug reaction

We Take a Lot of Drugs



20% of people over 65 take 10 or more drugs every day

Personalized Medicine: Genetic Tests For Drug Prescription

Problem:

- Over 100,000 deaths per year are due to adverse reactions to prescription drugs

Solution:

- For ~200 common drugs there is genetic guidance on the package insert
- Not used currently because the doctor does not know the genetic profiles of his patients
- Can use a simple genetic test to guide drug prescription

A Drug Package Insert Containing Genetic Guidance for a Gout Medication!

The Gout – Q&A & Treatment Options "One of the most painful conditions experienced by humans" – Choi HK et al.[1]   Prepared by: Z Dumont; B Jensen, L Regier © www.RxFiles.ca Apr 14

Gout: Overview of Causes, Risk Factors & Incidence[2]

- **Uric acid crystals** may deposit in joints, nephrons & tissues needle like, negative birefringent[3]. {↑serum uric acid (SUA) may contribute (>405μmol/L; theoretical saturation concentration)}
- **Pathophysiology**: ↑SUA: from ↓uric acid excretion 85% or ↑ purine breakdown; most commonly secondary 70% to drugs (chemotx, diuretics, ASA) disease (malignancies, renal dysfx, psoriasis), & dietary causes (beer, fish, red meat).
- **Risk factors**: ♂, CKD, HTN, obesity; hyperglycemia, hyperlipidemia, lead {Gout should prompt screen for conditions associated with CV risk!}[4,5,6]
  Precipitating factors: trauma, surgery, alcohol, starvation, ↑ purine foods & certain medications see Drug Induced.
- **Incidence**: <1%; mostly elderly, ♂ & postmenopausal ♀[7,8]. Prevalence: ≤7% in ♂ >65; ≤3% in ♀ >85[3].

What are the stages and diagnostic criteria for gout?[3]

1) **Asymptomatic hyperuricemia**: ♂:>360-420μmol/L; ♀:>357μmol/L[7] estrogen effect
   - <25% go on to develop acute gout[7,9]. ↑ if SUA ≥500 μmol/L, >600μmol/L incidence ~6%[10].
   - ***Usually* does not require drug treatment!** [9,10,25,33]
2) **Acute gouty arthritis**: quick onset 6-12hrs, *intense pain*, redness, heat & swelling, usually of one joint 90% of 1st attacks (commonly the big toe 'podagra' 50%, ankle/foot, knee, finger, but also the olecranon, helix of the ear, &/or nephrons – uric acid tends to crystallize in the cooler parts of the body), pain peaks at 8-12hrs; often skin desquamation over affected joint / tendon. (May self-resolve in 3-7-14d [9,10]). SUA ↑or normal![7] **Elderly**: less pain; ↑ polyarticular, fever & delirium.
3) **Intercritical gout**: disease may progress despite symptom free period(s). {symptom free periods may decrease over time; initially may be years symptom free [10].}
4) **Chronic tophaceous gout**: tophi progression to, bony erosions - deformations, nephropathy - stones

What is the concern of diuretics with gout?

- Loop e.g. furosemide & thiazide diuretics ↓excretion & ↑concentration of uric acid.
- Hydrochlorothiazide induced gout: ~1%[11]; risk ↑ when dose ≥25mg/d[12] Low dose thiazide (e.g. HCT12.5mg) often tolerated in patients with gout hx

What non-pharmacological therapies are recommended?

- **Acute attack**: rest, elevate limb, ice[13], avoid contact
- **Maintenance**: useful & may ↓ the need for preventative medications
  Diet: compliance with low purine diets is poor[14], recommend one less portion of meat or fish/day; drink wine instead of beer; drink a glass of *skimmed* milk each day.[15] Low fat dairy, fibre, ?Vit C, ?cherries & whole grains assoc. with ↓ gout.
  Low calorie diet more beneficial/acceptable than low purine diet!
  Avoid: liver, kidney, shellfish, gravy, sardine, sweetbread, Fructose[16], & yeast extract.
  Lifestyle: Weight loss!!! Smoking cessation! ↓ alcohol binging (especially beer)!
  ⇨ drink 2L water/day (unless CI'd), mild-moderate intensity exercise.

Are there any special treatment considerations?

- Lifelong tx may be required; however re-assess need for tx if attack free for many years &/or risk factors reversed; SUA levels may be useful[17].
- **Renal dysfx & very elderly**: adjust dose for allopurinol & colchicine; consider using colchicine or corticosteroids[18] as alternatives to NSAIDs.
- With NSAIDs, GI prophylaxis should be considered if history of PUD/GI bleed or ↑GI risk age>70 {**PPI** omeprazole 20mg daily $32; or misoprostol 200mcg bid-qid $38-49}
- Review CV risk due to association of gout with CVD; CV protection with ASA 81mg po daily if 2° prevention; benefit supersedes the ↑risk of gout attacks.

What are the primary drug treatment options for gout? ACR'12

- **Acute attack**: *Rapid treatment initiation is key: <24-48hr.*
  {Agent choice dependent on patient (severity, CI, DI, hx, SE, etc.) [e.g. consider HF, renal fx, GI ulcer hx, diabetes, transplant hx, previous tx, age, DIs.]}
  - **Colchicine** (eg. 0.6mg BID x1-3 days, then daily); stop after ≥1-2wk (start within 36hrs) {**FDA July/09**: 1.2mg po immediately, then 0.6mg once in 1hr RCT}
  - **NSAIDs** – Full/high doses to achieve pain relief until 48hrs after symptom resolution (or ~3 days); then stop or taper over 1-2 weeks
  - **Corticosteroid** IM methylprednisolone, PO prednisone (or Intra-Articular Betaject, Aristospan)[18,19,20] {May add acetaminophen to corticosteroid if NSAIDs & colchicine CI'd[21]}

  NOTE: Do not start, stop or adjust **allopurinol** during an acute attack!
- **Maintenance/Prophylaxis**[22]: Motivation to take meds may wane over time if no symptoms.
  - 1st attack: lifestyle changes & remove drug causes if possible
    Treat if: 1) recurrent attacks (≥2/yr); 2) ↑SUA levels >800μmol/L; 3) chemotx; 4) advanced dx tophus/tophi or urolithiasis; 5) CKD ≥Stage 2
  - 1st Line: **allopurinol**[23] (Start low, go slow, & prophylax as below!)
    - ➤ **Consider waiting 1-2wks after inflammation settles before initiating allopurinol** (fluctuating SUA, prolong attacks, may destabilize crystals)
    - ➤ **Prophylax with colchicine** low dose **or an NSAID** not ASA[24] **while titrating/adjust allopurinol** (usually ~ 3 – 6+ months[17]) **unless CI'd**
    - ➤ **Target SUA levels: <300 to 360μmol/L**[1,7,17]. Lifelong treatment.
  - **Alternative: colchicine** (low dose ≤ 0.6mg daily); may not prevent complications {Alternative: probenecid rarely an option SAP access, but requires renal fx ≥50ml/min} ACR'12

Generic/TRADE (Strength & forms) g=generic	Class / Pregnancy category[25]	Side effects / CI: Contraindications	√ = therapeutic use / Comments / Drug Interactions DI / Monitor M	Dosing: {for acute tx with NSAID or colchicine, Initial x 1-3 days ⇨ Follow-up x1-2+ wks}	$/30d
Naproxen NAPROSYN,g ALEVE OTC 125,250,375ς,500ς,750mg SR tab 500mg supp, 25mg/ml susp; OTC	NSAIDS (non-ASA) -↓pain & inflammation [P1 P3 L]	Common: n/v (Indomethacin: GI upset, headache, ↑SE especially CNS, & in elderly) CI: ↓ Renal (Stage ≥IV CKD), GI ulcer, HF, transplant Precautions: CVD; (Avoid Indocid ≥65yrs)	√ Gout – for acute attack or when initiating allopurinol GI prophylaxis (if indicated) with a PPI or misoprostol[17] DI: Li++; ACEI/ARBs (minor DI, except ↑K+ if on NSAID, spironolactone & ACEI or ARB) M: follow-up 4-6wks after acute attack to assess need of further tx; if at renal risk Na+ @24hr, SCr @72hr {Can use in CKD stage 1-2 & dialysis; avoid in stage 3 if CrCl ≤40ml/min & CKD stage 4.}	500-750mg x1; 500mg BID; ⇨ 250-500mg BID Max ≤ 1500mg/d x1day/short term. ⇨ Usual Max 1000mg/d	16-20
Ibuprofen MOTRIN, ADVIL,g 300,600mg tab;(200,400mg) OTC	For more info on NSAIDs, Acet, & Coxibs, see RxFiles PAIN charts at www.rxfiles.ca			600-800mg po TID; ⇨ 400-600mg TID Max 2400-3200mg	12-21
Indomethacin INDOCID,g 25,50mg cap; 50,100mg supp		{Indomethacin used historically; however others effective & less CNS SE's!}	Acute: High doses for 1st 24-72hrs of attack. Then stop, or use lowest effective dose over 1-2wks.	25-50mg po TID; ⇨ 25mg BID-TID Max 200mg/d {Historically used but other NSAIDs now preferred.}	14-23
Celecoxib CELEBREX 100,200mg cap	COX-2 specific inhibitor -↓ pain & inflammation [P L]	Common: GI maybe less than some other NSAIDS CI: CVD, Renal dysfx Precautions: GI ulcer	√ Gout–acute attack or when initiating allopurinol DI: Li++, ACEI/ARBs M: follow-up 4-6weeks after acute attack to assess need of further tx	100-200mg po BID; ⇨ 100-200mg OD-BID Max 400-800mg/d	54
Acetaminophen TYLENOL,g 325,500,650mg tab ▼ OTC	Analgesic -↓ pain (minimally effective) [P L]	Common: rash Serious: hepatotoxicity Precautions: Liver dysfx &/or alcoholism	√ Mild gout associated pain &/or in combination with corticosteroids. DI: Warfarin if ↑ dose acetaminophen M: Liver function tests if long term & ↑EtOH intake	650-1000mg po q6h (prn; adjunct to CS) Max 4000mg/d	15-25
Colchicine COLCHICINE-ODAN,g 0.6ς,1ς mg tab [Colcrys USA] IV Colchicine not recommended →toxicity[10]	Anti-gout: ↓ pain, inflammation: ↓'s urate crystal deposition by: ↓leukocyte motility, phagocytosis, etc. Familial Mediterranean Fever 1.2-2.4mg/d 1° prevention: Postpericardiotomy Sx [P L]	Common: NVD 80% @high dose; 4-25% @low dose → ↓dose/stop; rash, alopecia. Serious: neutropenia, myopathy, liver, rhabdomyolysis. Precautions: CVD; ↓ renal fx ↓dose CI: blood dyscrasias, solid organ transplant; ? maybe dialysis	√ Gout – acute attack or if initiating allopurinol[24]; {SE with high doses however limiting to ≤3 tabs on 1st day then 1-2 tabs/day will ↓↓↓ diarrhea/GI side effects!!!} DI: cyclosporine ↑myopathy, P-gp & 3A4 inhibitors: clarithro & erythro-mycin, ketoconazole, verapamil, diltiazem, juice M: CBC neutropenia, Creatine Kinase rhabdomyolysis: may ↑ with statin/fibrate & renal fx q6mon	Initial: 1.2mg x1 stat, then 0.6mg in 1hr or 0.6mg po BID-TID x1-3 day ⇨ then OD x 7-10+ day. 0.6mg OD or BID for ~ 3 - 6+ months if starting allopurinol {If ↓renal fx, ↓dose to every other day if prolonged tx 10+ days}	12-17 16 - 26
Methylprednisolone acetate DEPO-MEDROL,g 20,40,80mg vial **Triamcinolone** acetonide KENALOG 10 & 40,g 10mg/ml 5ml, 40mg/ml 1ml, 40mg/ml 5ml vial [P L]	Corticosteroids/ -↓ inflammatory response Hydrocortisone SOLU-CORTEF 100,200mg vial	Common: inj site rx Serious: edema/HF; SE: Caution in long term, but rare in short term Precautions: systemic & viral infections, immunosuppression, local skin atrophy Glucocorticoid: Prednisone 5mg = Methylprednisolone 4mg	Useful if CI/SE's to NSAIDs & colchicine eg. for renal, transplant, warfarin pts, etc. √IM or IA inj x1: monoarticular attack √IM or oral: polyarticular attack DI: aprepitant ↑CS levels, vaccines DI: rare with intra-articular minimal systemic absorption M: osteoporosis risk if prolonged / frequent use; diabetes: ?? ↑BG testing (IA: suggest minimum 3 months between treatments) {Betamethasone {sodium phosphate & acetate: Fast acting & Long acting} BETAJECT 3mg/1ml vial IM/IA $9/vial} {Triamcinolone hexacetonide ARISTOSPAN 20mg/1ml vial peds; $7/vial}	IM: Methylprednisolone: 40-80mg IM x1 Pending age / degree of inflam IA: Small joints Phalanges: Methylpred 4-10mg IA; 8mg Triamcin 2.5-5mg IA; 10mg Betameth 1.5-3mg IA; 3mg IA: Large joints Knees/ankles: Methylpred 20-80mg IA; Triamcin 5-15mg IA; 40mg Betameth 1.5-3mg IA; 6mg	5-9/vial 9/1ml vial 5/1ml vial
Prednisone WINPRED,g 1,5ς,50ς mg tab (Prednisolone 1mg/ml susp) [P L]	Methylprednisolone MEDROL 4ς,16ς mg tab	Common: insomnia, ↑BP, ↑BG, GI upset, mood △ Serious: most rare in short term; edema/HF		25-50mg po daily x 3-5 days & stop[20]; no taper! {If catch early e.g. 1st sign, 10mg x1-2 may be adequate}	15
Prophylaxis: **Allopurinol** ZYLOPRIM,g 100ς,200ς,300ς mg tab [P L]	Xanthine oxidase (Xanthase) inhibitor -↓uric acid production -↓BP in young hypertensive pts -Adjunctive to K+ citrate for uric acid stones	Common: rash 2%, diarrhea Serious: Allopurinol hypersensitivity syndrome <1% (≤30% mortality! ↑risk if ↓ renal fx (e.g. ACEI, NSAID), elderly, diuretic use): start low! Stevens-Johnson Sx 28, ↑with HLA-B*5801-Asian CI: Acute gout Precautions: renal ↓dose or liver dysfx	√ Maintenance; adjust dose for SUA, renal fx, tolerability & response DI: rash maculopapular when used with ampicillin ~20%/amoxicillin; antacids, thiazide, ACEI; ↑ toxicity of 6-MP, azathioprine, cyclophosphamide & theophylline ↑; warfarin ↑INR M: SUA & renal fx q3mon 1st year then q6mon[10] (See CPS for dosing info in ↓renal fx) Note: Allopurinol desensitization[27] possible (susp ↑'s from ≤50ug to 100mg over ≥28day).	Start at 100mg; ↑100mg q2-4wks ↓risk of rash, etc. Usual dose: 300mg daily, preferably after food Usual range: 100-800mg (divide doses ≥300mg to ↓GI SE) If CKD, hepatic impairment, or elderly start 50mg/day; ↑ 50mg increments. MAX 300mg/d	15 10-26
Febuxostat ULORIC[28], New Canada, 80 mg tab	Xanthine oxidase inhibitor like allopurinol but unique structure [P L]	Common: ↑LFT 5-7%, nausea, arthralgia, rash Serious: ?MI, ?stroke	DI: azathioprine, didanosine, mercaptopurine, theophylline (↑levels of each) M: LFT (@2-4 mo, then periodically) Note: may ↓uric acid > allopurinol, but no less attacks	40-80mg tab po daily lack of data for use in CrCl <30ml/min More flares during initiation than allopurinol. Max 120mg/day	55

= ↓ dose for renal dysfunction ς=scored tab χ=Non-formulary Sask ⁓=Exception Drug Status Sask. ⊗=not covered by NIHB ▼=covered by NIHB Ø=NIHB EDS **ACEI**=ACE inhibitor **BG**=blood glucose **BP**=blood pressure **CI**=contraindication **CKD**=chronic kidney disease **CS**=corticosteroids **CVD**=cerebral vascular disease **DI**=drug interaction **dx**=diagnosis **fx**=function **GI**=stomach **HF**=heart failure **HR**=heart rate **HTN**=hypertension **hx**=history **IA**=intra-articular **Li**=lithium **M**=monitor **MI**=myocardial infarction **n/v**=nausea/vomiting **OTC**=over the counter **pt**=patient **SE**=side effect **SUA**=serum uric acid **sx**=symptoms **tx**=treatment **wt**=weigh

Uricosurics: (rarely used): Probenecid BENURYL,g D/C; SAP 500ς mg tab; 1g BID $34 (0.5-2g/d); SE: rash, GI upset; CI: nephrolithiasis Hx; renal: ineffective if CrCl<50mL/min; Drink 2L H_2O/d. DI:ASA, azathioprine, MTX. {Also Sulfinpyrazone ANTURAN g, 200mg tab; 100-200mg BID $17-27; no longer used.}
Other Meds for Tx: Oxypurinol[29] oral allopurinol metabolite in trial; losartan & fenofibrate[30]: modest uricosuric effect (potential losartan or calcium channel blockers if gout + htn); Opioids possible adjunct analgesic[31]; ACTH 25-40 IU SC[10]; Anakinra: 100mg SC daily x3days. **Goals**: ↓acute inflammation, prevent flares, ↓SU
Pegloticase: USA: Krystexxa urate oxidase enzyme, 8mg IV over ≥2hr q2-4wk, allergic rx, CI: G6PD, ↑↑ SUA; Benzbromarone ↑urate excretion; orally special access CDN[32] & Ketorolac IA inj; Rasburicase IV: USA for tumor lysis sx in cancer pt. CI: G6PD HERBAL: no documented efficacy; ?(caffeine[33], devil's claw & garlic). Anecdotal support: berry juice/ berri
Rule out: Pseudogout[34] (calcium pyrophosphate CPPD crystals in synovial fluid, commonly the knee), "Appears like OA, but in all the wrong places" possibly tx with colchicine 0.6mg/d or CS; Septic arthritis aspirate joint, WBC, temperature & vitals, do gram stain & culture; & Rheumatoid arthritis.
Drug induced: acetazolamide, ASA low dose, chemo, cyclosporine, diuretic, ethambutol, lead, levodopa, niacin, tacrolimus, teriparatide, ?ticagrelor **Food induced**: purine rich eq. red meat, fish, beer, spirits **Diagnosis**: Diagnostic certainty→ analyze synovial fluid for uric acid crystal or id'ing tophus containing uric acid crystal under polarized light microscopy. May see "mouse bite" erosions. Optional 24hr urine collection: to see if ↓excretor or ↑producer[3,10] but does not alter tx; (if uric acid excretion ≥1g with reg. diet→over-producer, if CL uric acid <6mL/min→under-excretor) since allopurinol effective for both[1].
Diagnostic Rule Variables: male sex, previous patient-reported arthritis attack, onset within 1 day, joint redness, first metatarsophalangeal joint (MTP1) involvement, hypertension or ≥1 cardiovascular disease, & serum uric acid level >350umol/L. www.umcn.nl/goutcalc Janssens'10 68

Personalized Medicine: Genetic Tests To Avoid Adverse Reactions to Prescription Drugs

GenXys Healthcare Systems

Genetic test (in EMR)

Physician diagnosis

Computer algorithm

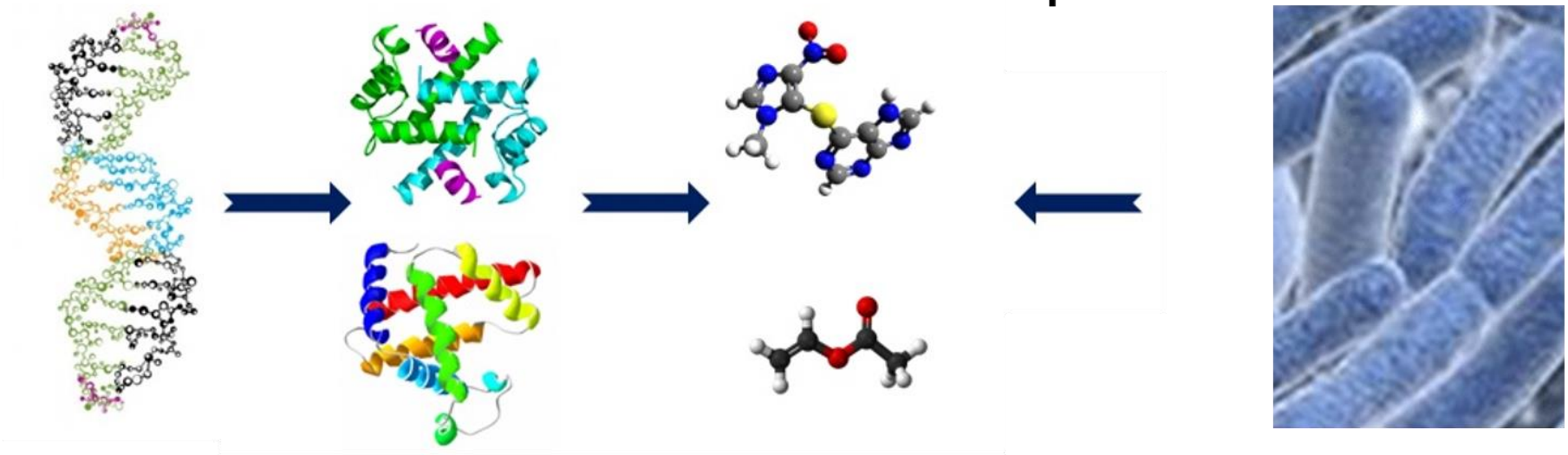
Personalized prescription

Fewer adverse drug reactions,
More efficient healthcare

We Can Measure Much More About You Than Your Genetics

You: Your genes code for proteins which produce metabolites

Your environment: Your microbiome produces proteins that produce metabolites



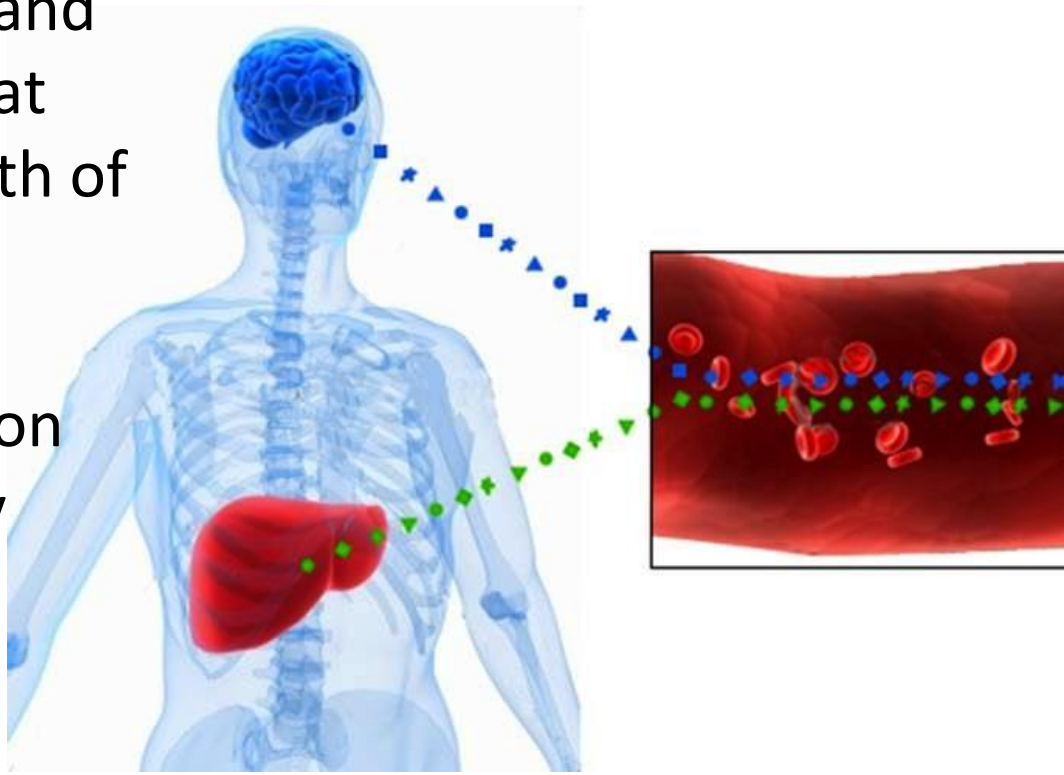
Genomics **Proteomics** **Metabolomics** **Microbiomics**

The "Omics"

Your Blood Contains Many Proteins and Metabolites That Can Be Used to Detect and Diagnose Disease

Each organ secretes proteins and metabolites into the blood that can be diagnostic for the health of that organ:

- Early detection of disease
- Monitor disease progression
- Monitor effects of therapy
- Detect re-occurrence of disease

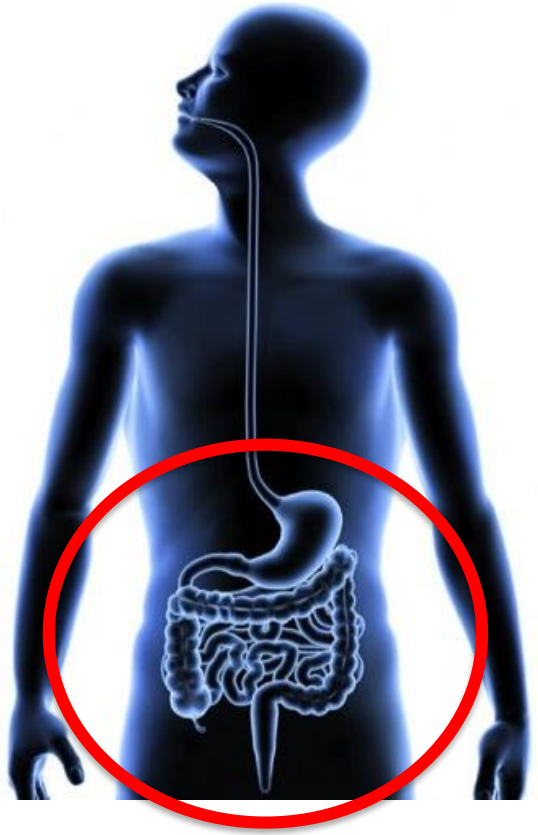


We can now detect hundreds of proteins and metabolites in your blood simultaneously to diagnose disease anywhere in your body

Your Microbiome: Bacteria Living In and On Your Body Can Also Influence Your Health

You contain 10 times as many bacterial cells as human cells; your “microbiome”.
The wrong microbiome can contribute to:

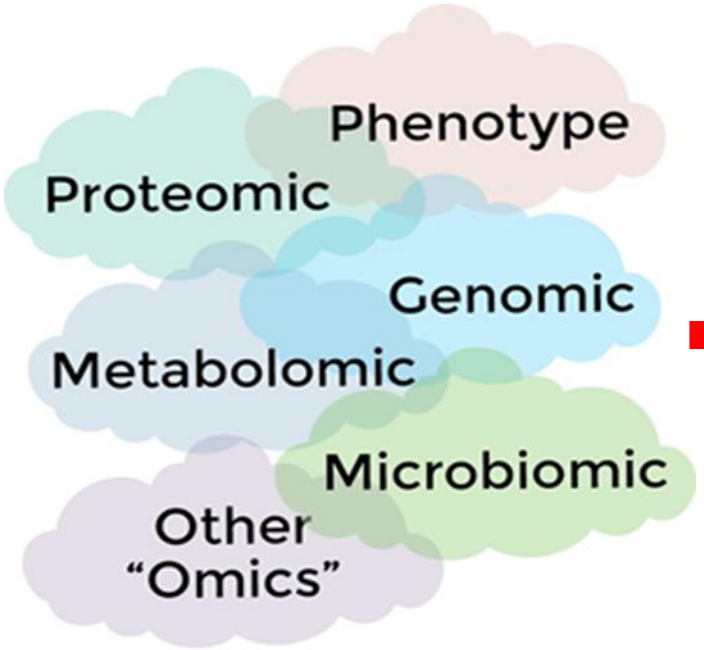
- Inflammatory bowel disease
- Diabetes
- Rheumatoid arthritis
- Muscular dystrophy
- Multiple sclerosis
- Obesity
- Autism (?)



We can measure a thousand or more bacteria in your gut (fecal sample) to characterize your microbiome

The Future of Medicine: “Omic” Profiling To Enable Personalized Medicine

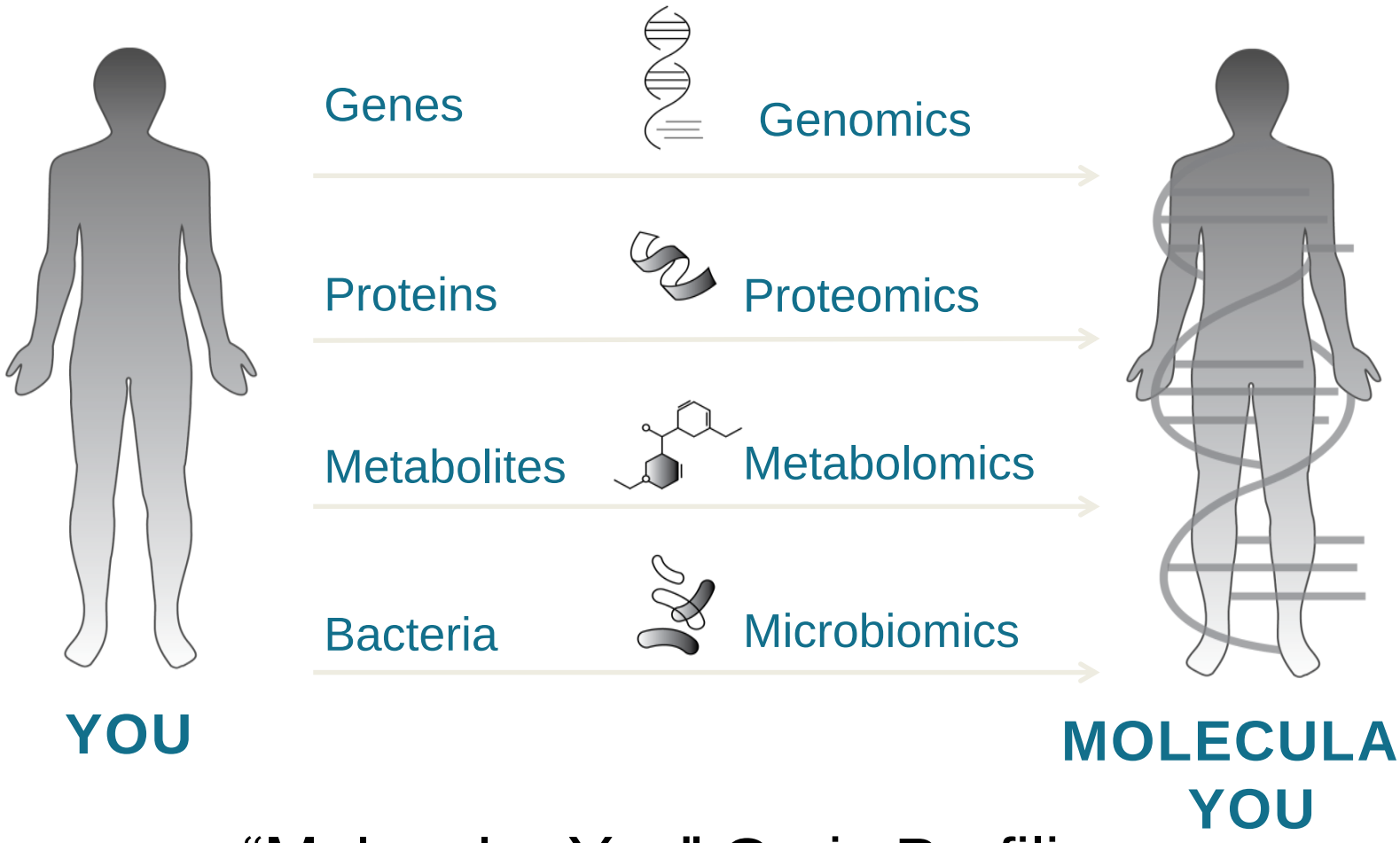
Well people, disease cohorts



Molecular data-clouds for each individual

- Early detection of disease
- Disease stratification
- Better matching of treatment to disease
- Identification of new biomarkers/targets associated with disease
- Effective preventive medicine

We Started A Company To Do Molecular Profiling: The Molecular You Corporation



"Molecular You" Omic Profiling

How Many Molecules and Bacteria Can We Measure?

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Genetic Profile

Analysis of genome sequence:

Whole exome

ONCE

Protein Profile

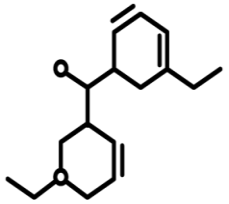
Analysis of proteins in the blood:

240 proteins

Microbial Profile

Analysis of bacteria in gut :

~1,000 bacteria



Metabolite Profile

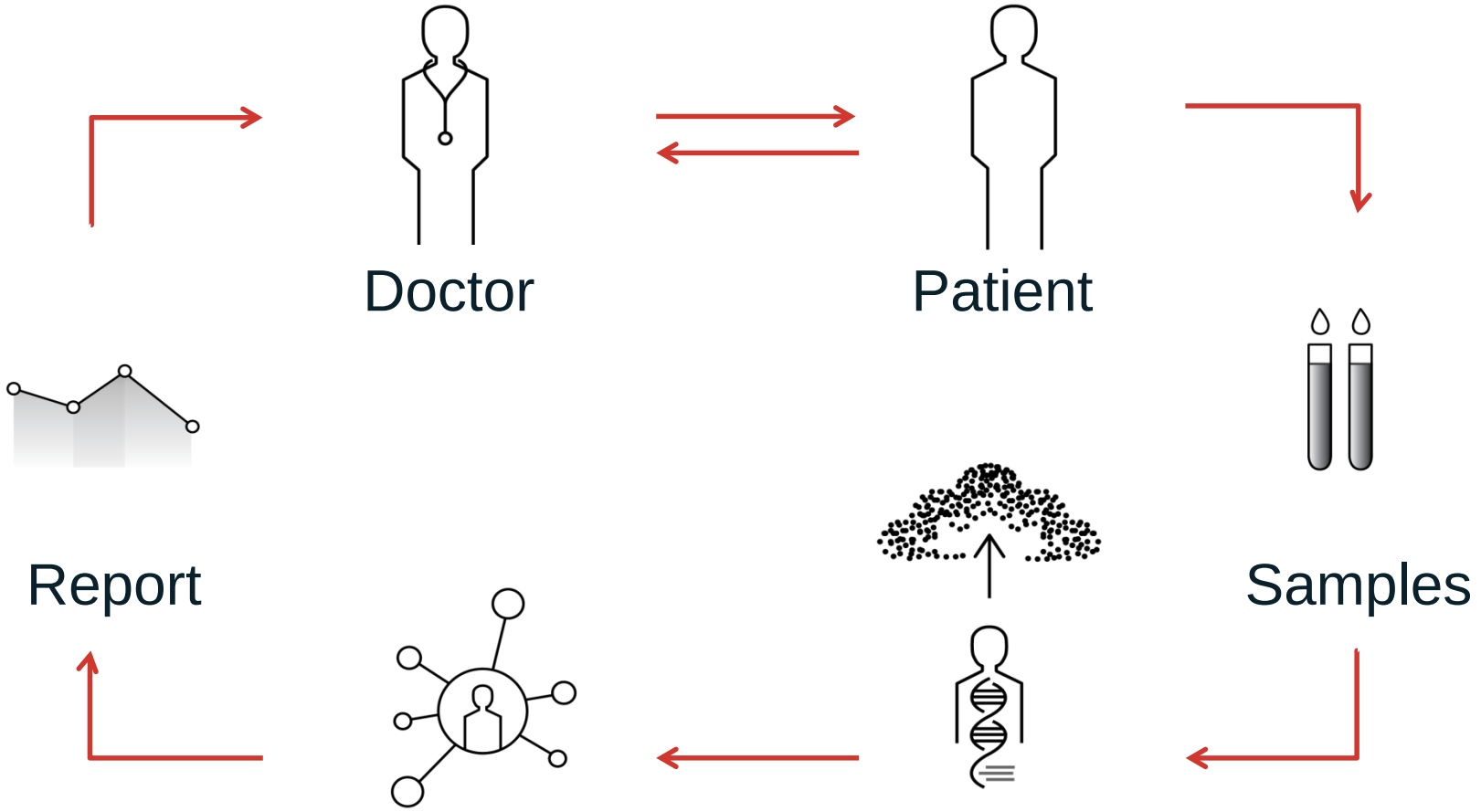
Analysis of small molecules in urine and blood:

~300 metabolites

FREQUENCY DETERMINED BY PARTICIPANT AND PRACTITIONER

This is just the start!

The Molecular You Process



Your Data Cloud is Compared to a Curated Reference Database

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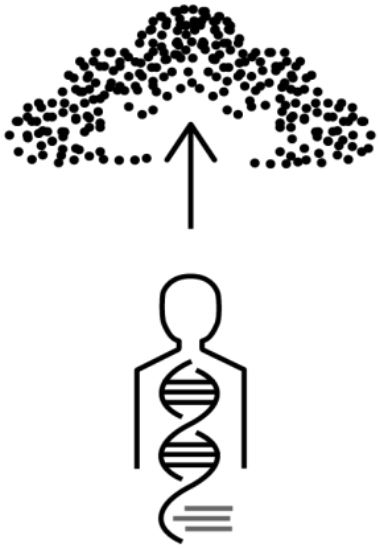


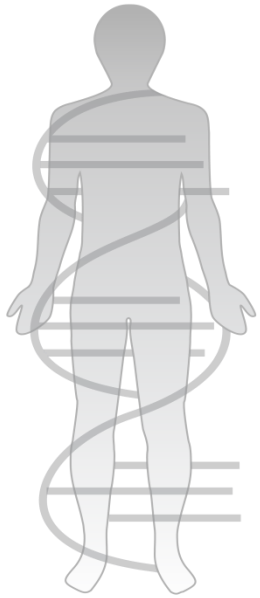
World's clinical information: Omic biomarkers associated with more than 300 diseases (1-12 studies per disease)

Disease-associated outliers

"Big data" storage and analytics

The Molecular You Analysis Provides Diagnostics/Risks for >300 Diseases

- Heart disease
- Diabetes
- Hypertension
- Stroke
- Breast cancer
- Prostate cancer
- Colon cancer
- Lung cancer
- IBD
- Pancreatic cancer



MOLECULAR YOU

- Dementia
- Depression
- Autism
- Osteoporosis
- Arthritis
- Kidney disease
- Pneumonia
- COPD
- Multiple myeloma
- Leukemia
- etc

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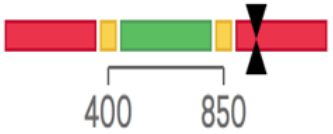
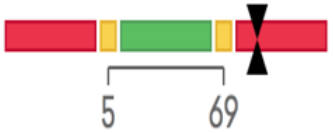
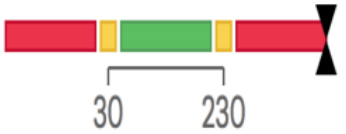
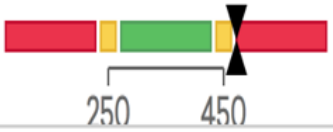
The Molecular You Analysis Provides Diagnostics/Risks for >300 Diseases

Disease score: number of molecular measures outside normal range that correlate with a particular disease

NAME	SCORE
Diabetes	17.5
Obesity	8
Insulin resistance	7
Metabolic syndrome	4.5

The Molecular You Analysis Provides Diagnostics/Risks for >300 Diseases

Can examine your data to see what the molecular measures are and what they should be

MEASURE NAME	CURRENT VALUE	VALUE WITHIN RANGE
Alpha-2-HS-glycoprotein	1032.84 µg/mL	
Apolipoprotein C-II	95.6 µg/mL	
Apolipoprotein C-III	529.9 µg/mL	
Fibronectin	464.4 µg/mL	

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Analysis of Your Molecular Profile Leads to a Detailed Health Status Report and Action Plan

Dashboard for your health

- Level 1: Overview
  - a top line summary of your health
- Level 2: Disease risk report (>300 diseases)
- Level 3: Organ/system health summary
  - Brain, GI tract, heart, immune system, joint/muscle, kidney, liver, etc
- Level 4: Details of organ/system health
  - Scientific literature

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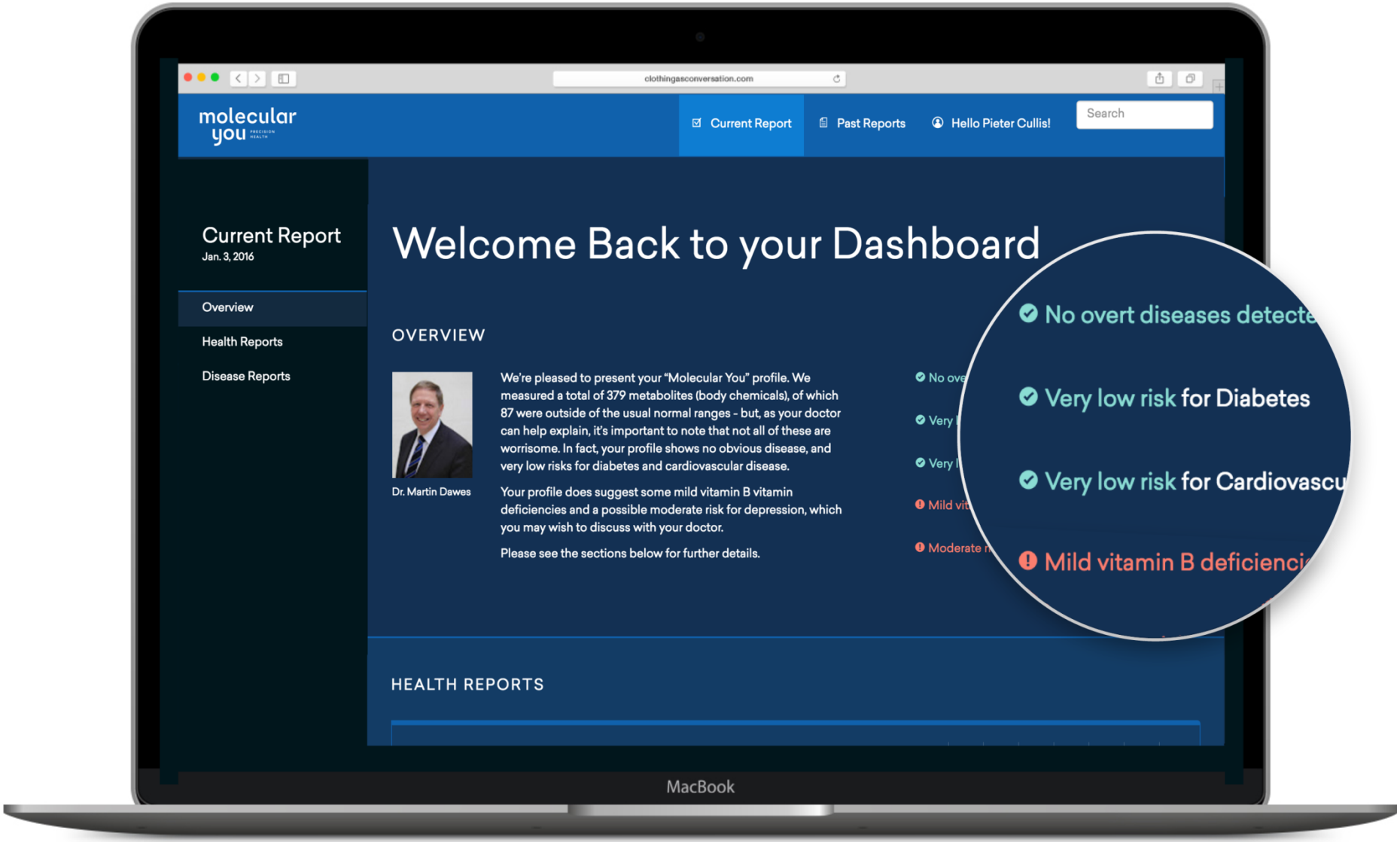
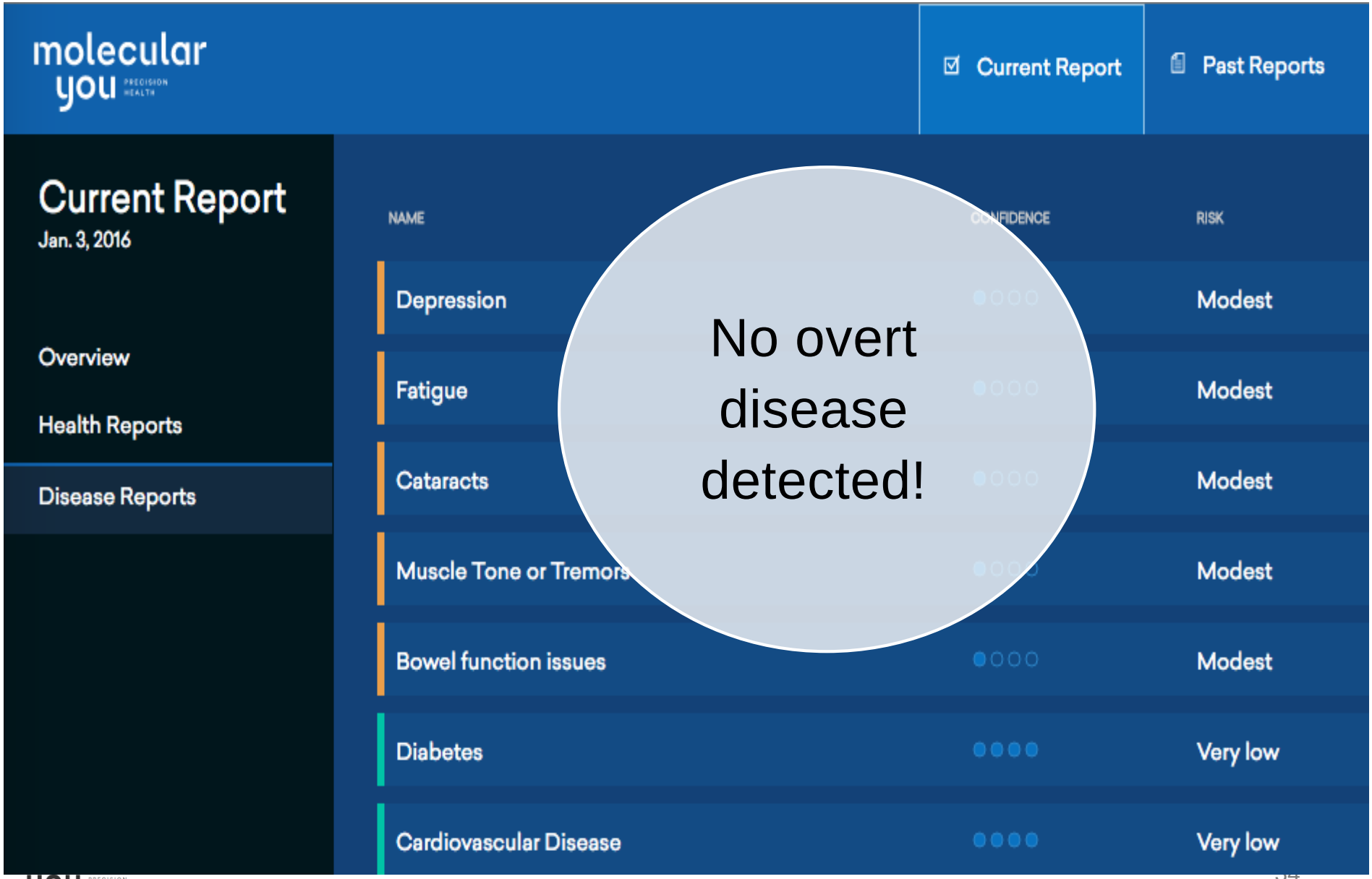
The MYCO Report: Overview



The MYCO Report: Disease Diagnosis/Risk Report



The MYCO Report: Organ/Nutritional Health Reports

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Brain health is on the low side.

The MYCO Report: Brain Health

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Both carnosine and serotonin levels are low

The MYCO Report: Nutritional Health

Vitamin B1 and B3 levels are low

The MYCO Health Action Plan

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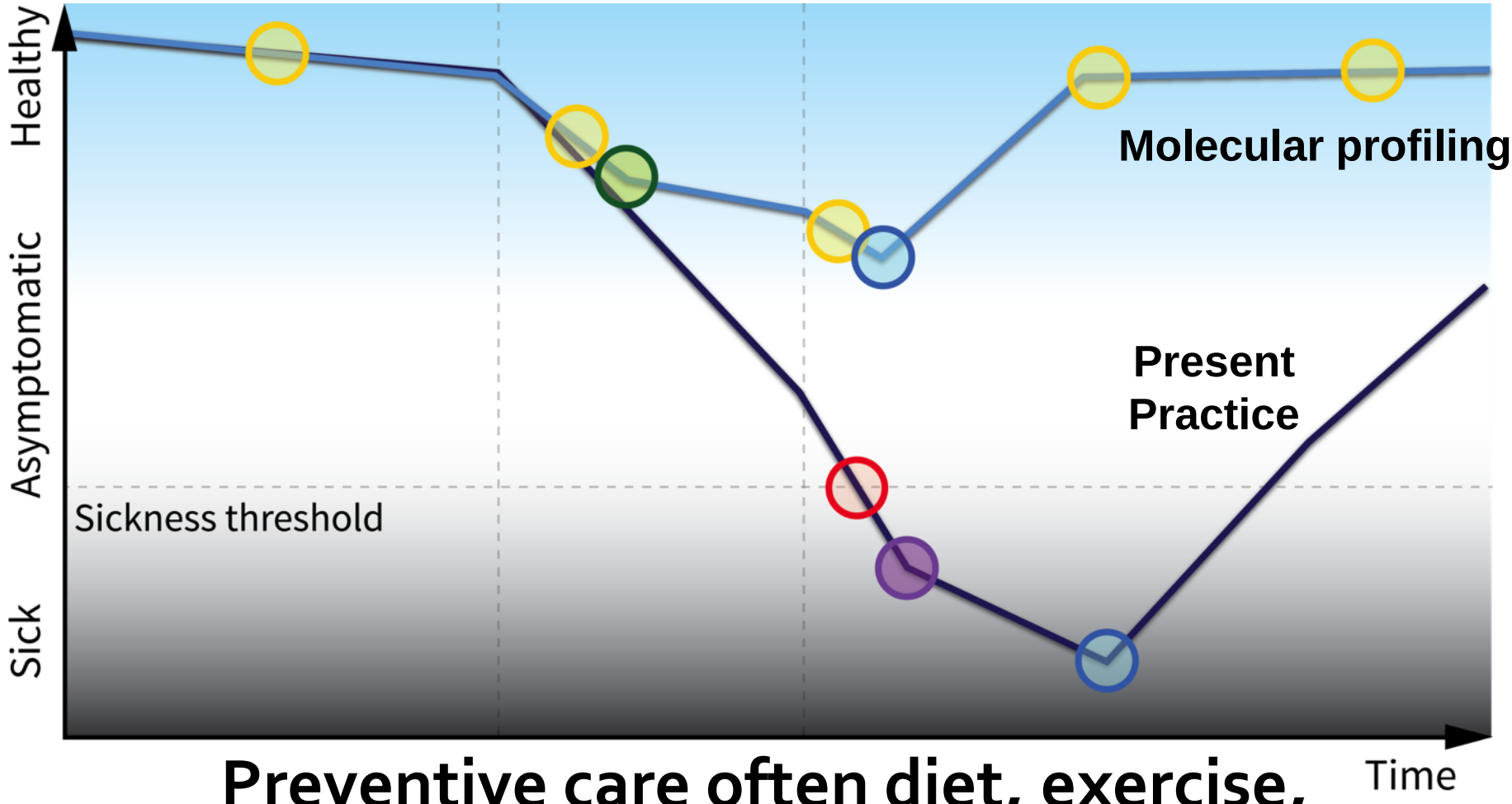
Early Detection of Trends Towards Disease Will Allow Effective Preventive Care



Preventive care often diet, exercise, supplements

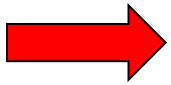
Personalized Medicine Will Revolutionize Healthcare

Molecular Profiling

Detection of early stage disease

Accurate diagnosis of disease

Targeted therapy



Benefits

Patient empowerment

Effective, non-toxic therapy

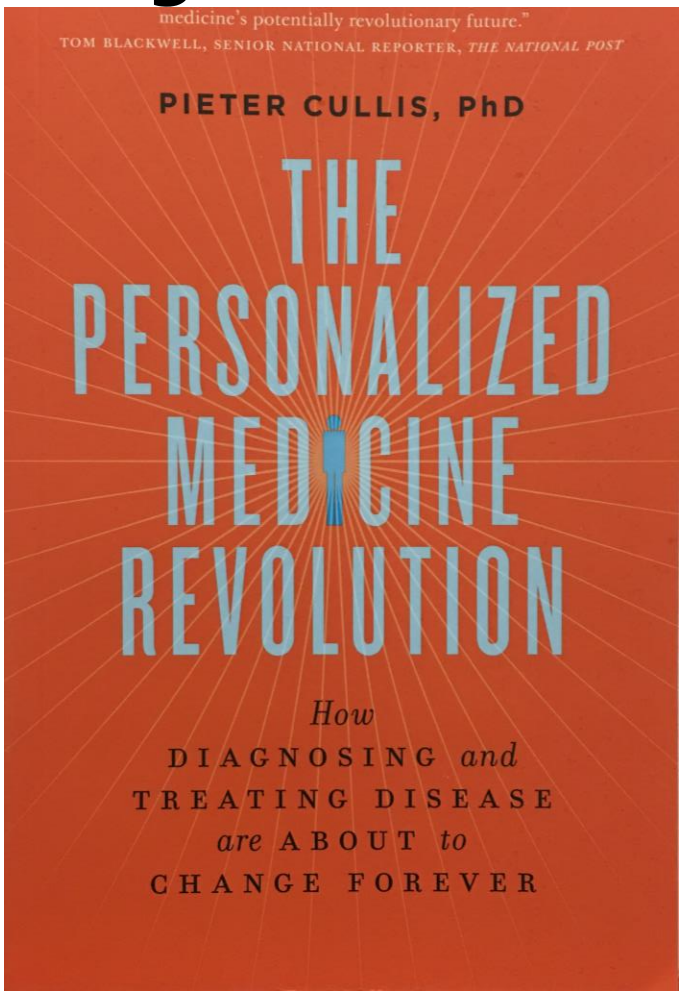
Effective preventive care

The Revolution Has Already Started

Top 5 events in Personalized Medicine in 2015-16:

- More than 100,000 people have had their genome sequenced
- Cancer therapy increasingly dictated by the genetic makeup of the tumour as opposed to location (breast, prostate, lung etc) of the tumour
- First introductions of genetic tests in drug prescription and cancer therapy to avoid adverse drug reactions
- Personalized immunotherapies for leukemia
- **Omic profiling to guide individualized healthcare**

"The Personalized Medicine Revolution: How Diagnosing and Treating Disease Are About to Change Forever"



If you want to buy it, go to Amazon.com