



Genomics Impact on Pharma R&D: Next Generation Drugs, Co-Diagnostics and Patient Solutions

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Our Vision

To eliminate disease through developing highly innovative medical solutions for people around the world



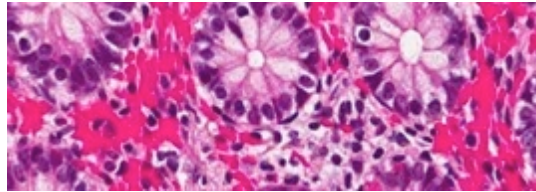
Research Strategy

- Focus on areas of highest unmet need & compelling science
- Integrate internal & external science
- Companion diagnostics
- Disease interception approaches
- Patient solutions



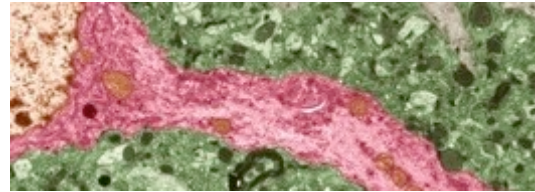
Creating Value Through Innovation

End-to-End Strategy Focused on Five Therapeutic Areas



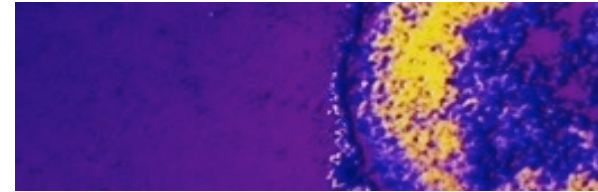
IMMUNOLOGY

- Inflammatory bowel disease
- Rheumatoid arthritis
- Psoriasis
- Pulmonary



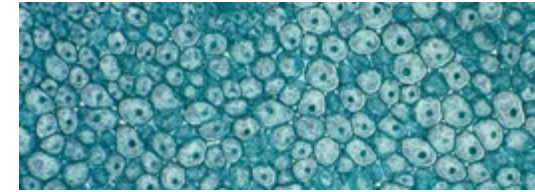
NEUROSCIENCE

- Alzheimer's disease
- Mood disorders
- Schizophrenia
- Chronic pain



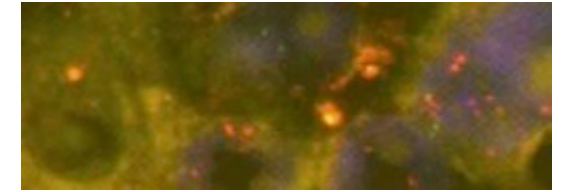
INFECTIOUS DISEASES & VACCINES

- HIV
- HCV
- Respiratory
- Vaccines



CARDIOVASCULAR & METABOLISM

- Cardiovascular disease
- Diabetes



ONCOLOGY

- Prostate
- Lung
- B-cell malignancies

GENOMICS/INFORMATICS/BIOMARKER DISCOVERY

JANSSEN COMPANION DIAGNOSTICS

FDA Approved Oncology Companion Diagnostics

- Single gene markers or mutations in the drug target (or gene) in the targeted signaling pathway
- No complex molecular profiles approved yet as companion diagnostics
 - Need very large sample size at efficacious dose to detect reproducible profile
 - Challenges with obtaining sufficient tumor samples
 - Challenges with assay sensitivity
 - Ph 2 endpoints (tumor shrinkage) don't always translate to Ph 3 endpoints (survival)

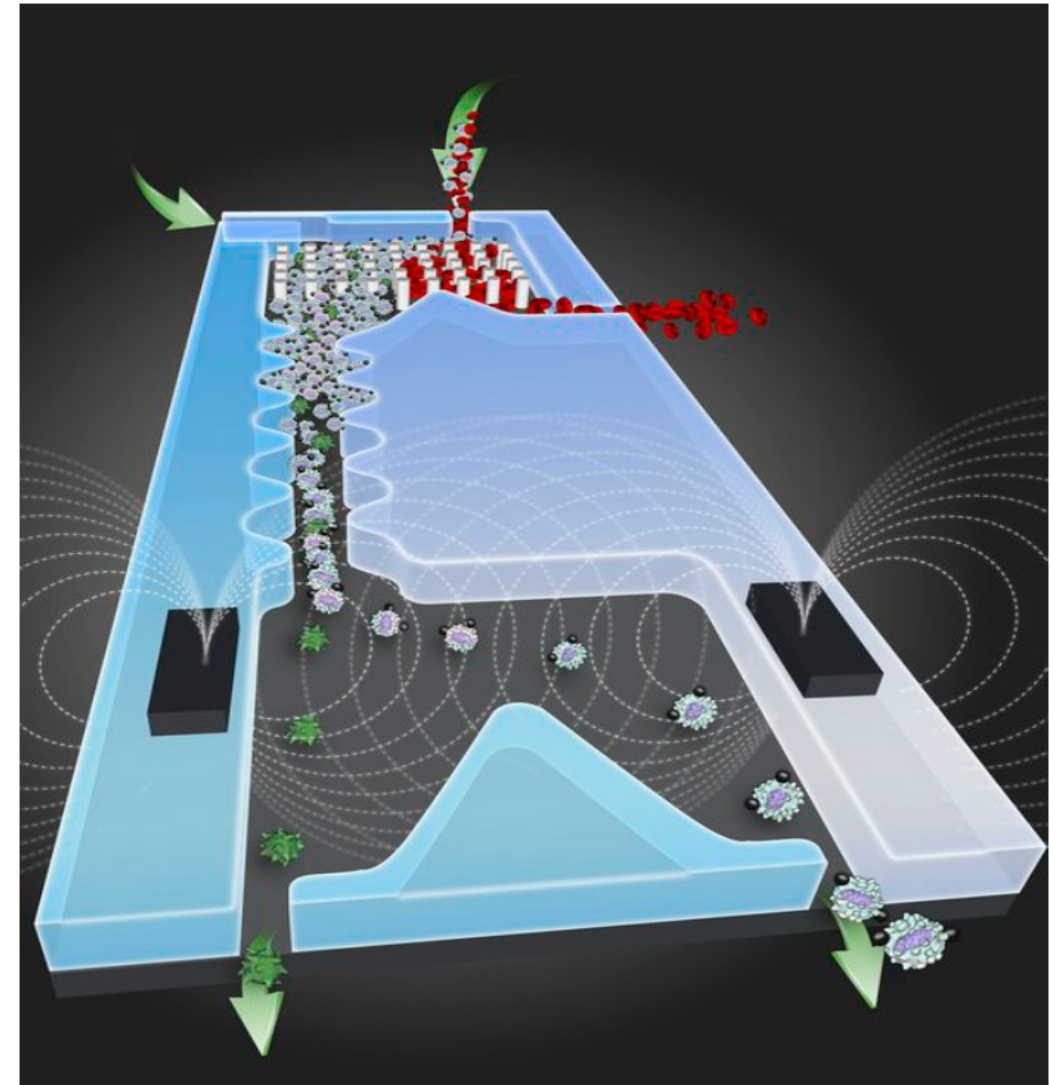
Date	Drug	Markers
1998	trastuzumab	HER2
2007	lapatinib	HER2, EGFR
2001	imatinib	BCR-ABL, KIT
2006	dasatinib	BCR-ABL
2007	nilotinib	BCR-ABL
2004	cetuximab	KRAS
2006	panitumumab	KRAS
2011	crizotinib	EML4-ALK
2011	vemurafenib	BRAF
2012	pertuzumab	HER2
2012	bosutinib	BCR-ABL
2012	ponatinib	BCR-ABL
2013	dabrafenib	BRAF
2013	trametinib	MEK

Circulating Tumor Cells (CTC): Advancing Towards Personalized Medicine in Oncology

- CTC numbers are prognostic for disease outcomes & treatment response
- Next gen device will enable CTC capture and characterization
- Tumor molecular profiling at diagnosis and relapse

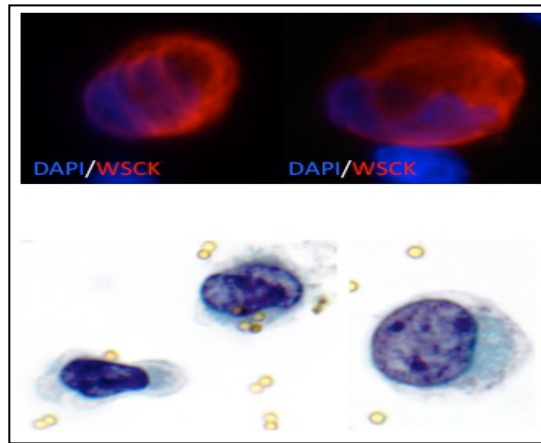
de Bono JS, Scher HI, Montgomery RB, et al. *Clin Cancer Res.* 2008;14(19):6302-6309

Ozkumar *et al.*, *Science Translational Medicine* 5:179 ra47, 2013

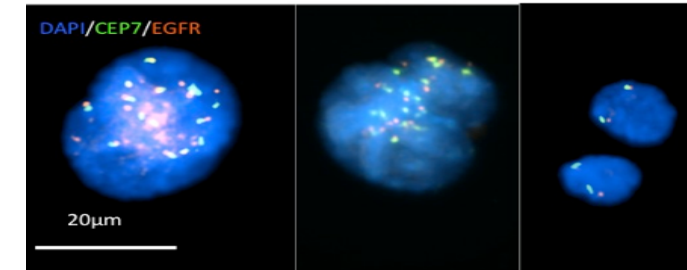


Next Generation CTC Platform

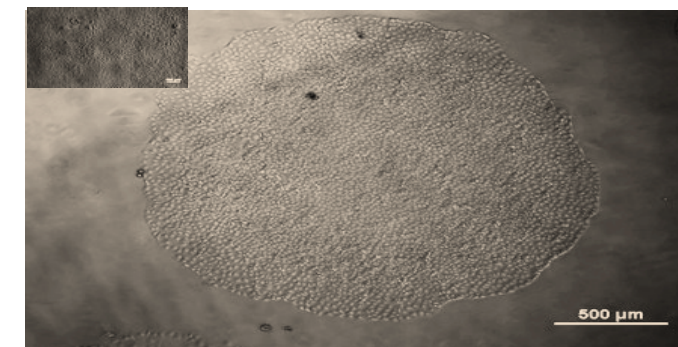
Non-Invasive, Real-Time CTC Characterization



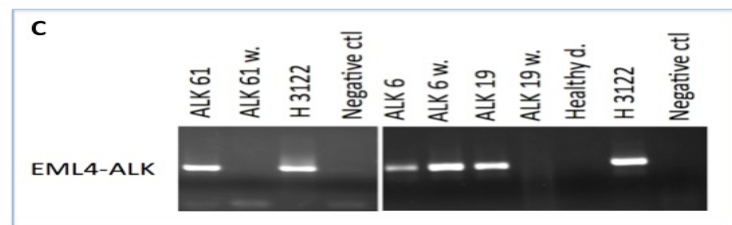
Cell Morphology & Gene Expression



Chromosomal Abnormalities

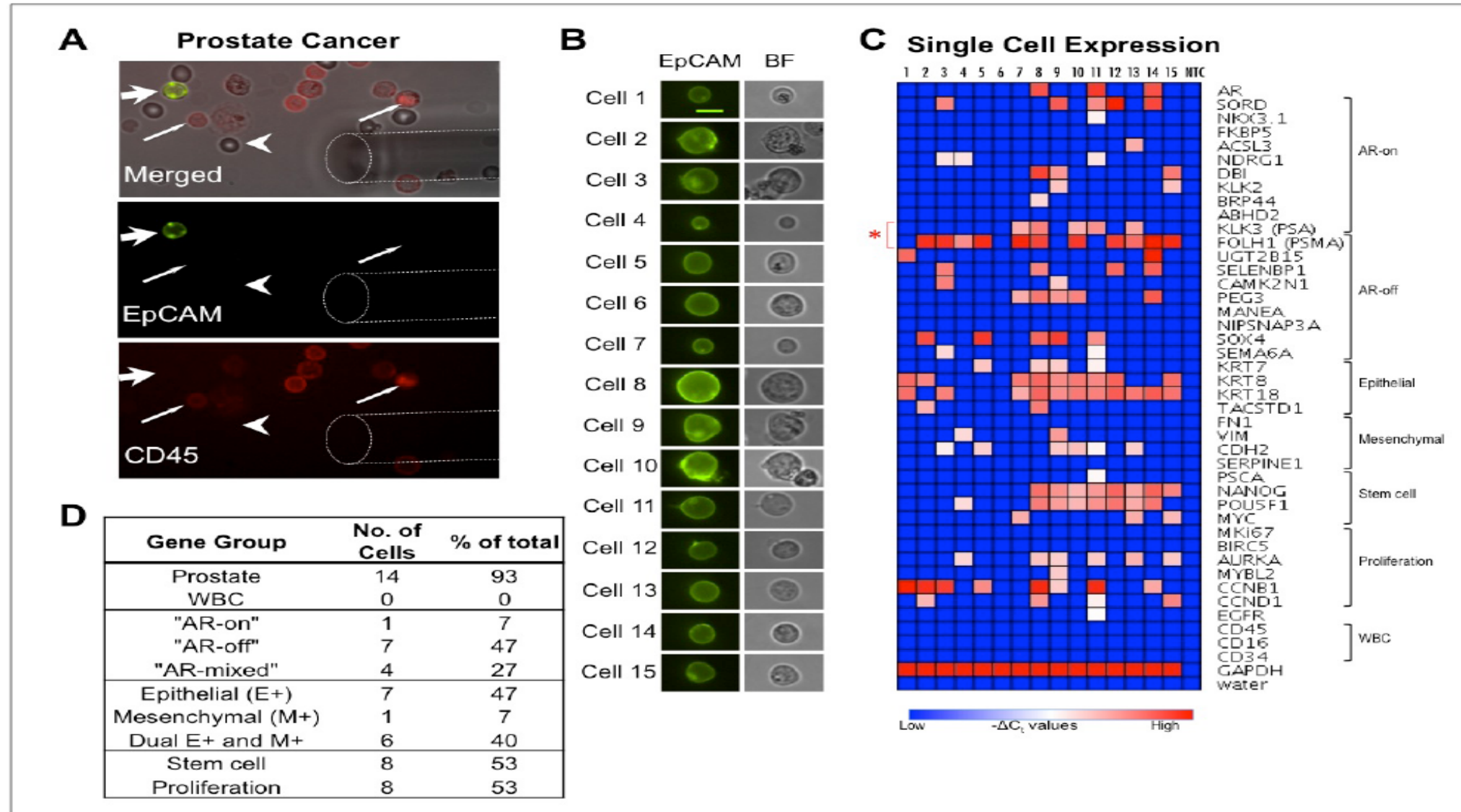


ex-vivo culture



Molecular Characterization

Single Cell Analysis Reveals Tumor Heterogeneity

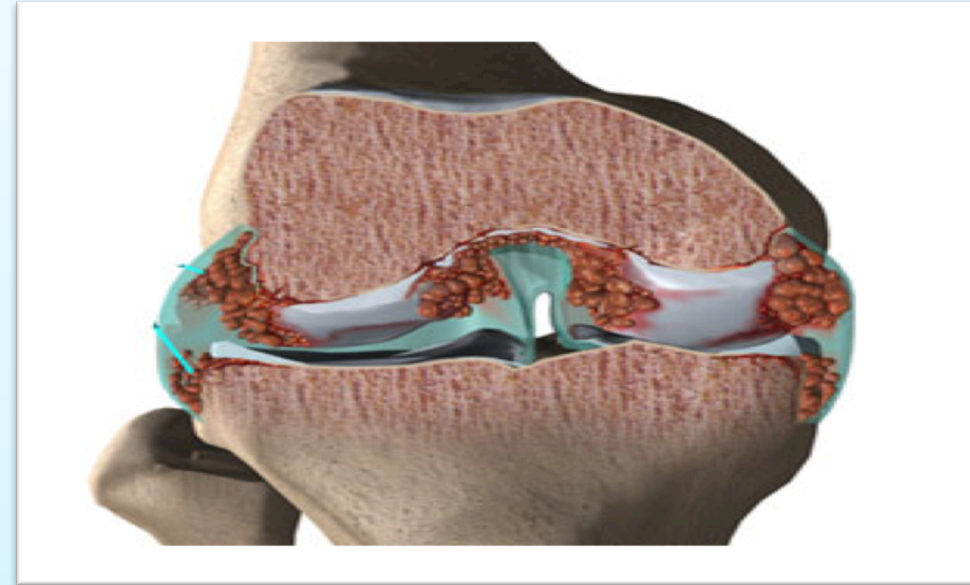


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Rheumatoid Arthritis: A Destructive and Debilitating Systemic Immune Disease



Early swelling leads to severe pain, and disability that is partially reversible

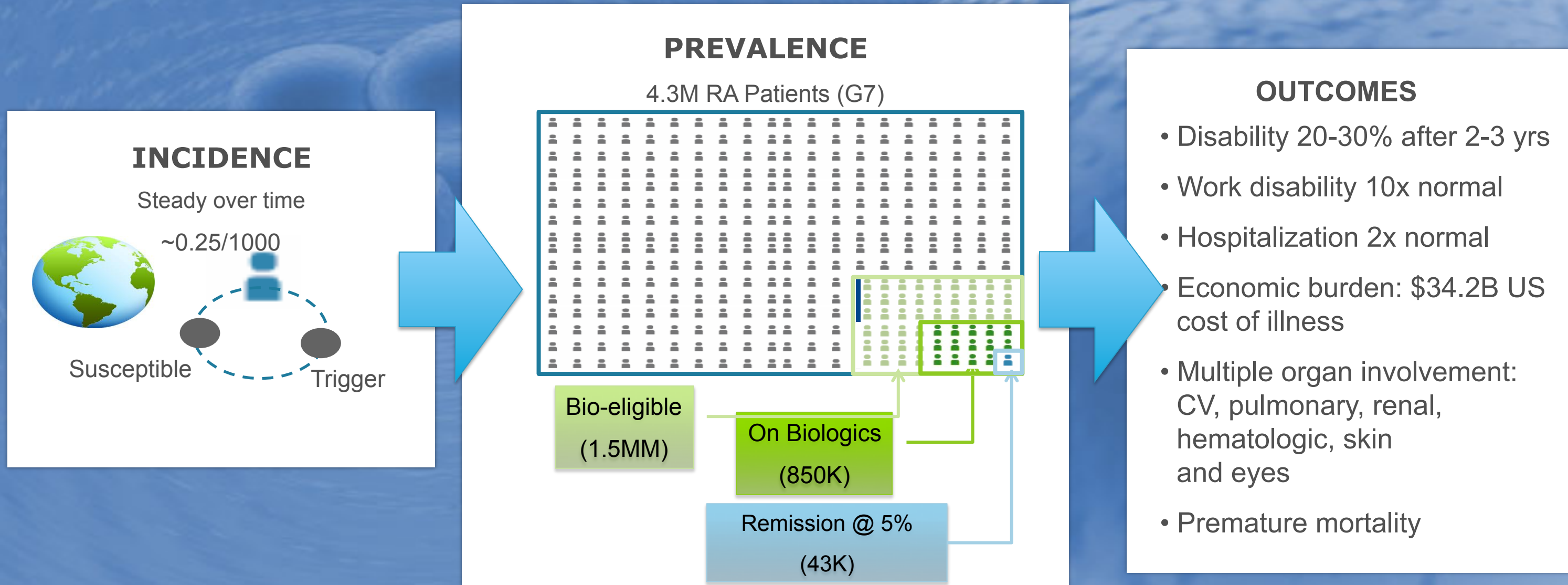


Synovitis leads to joint destruction, loss of function and decreased quality of life



Chronic inflammatory response results in joint structure degradation, permanent disability and co-morbidities including lymphoma and CV disease

Few Rheumatoid Arthritis Patients Achieve Complete Remission



RA Treatment Paradigm Shifts



Prognostic Markers



Predictive Biomarker Co-Dx



Monitoring Biomarker Dx



Disease Interception

Network Pharmacology
Early Disease Identification

Best drug for initial treatment

Digital Health Care
Optimize Patient Outcomes

New Therapies
Novel Mechanisms

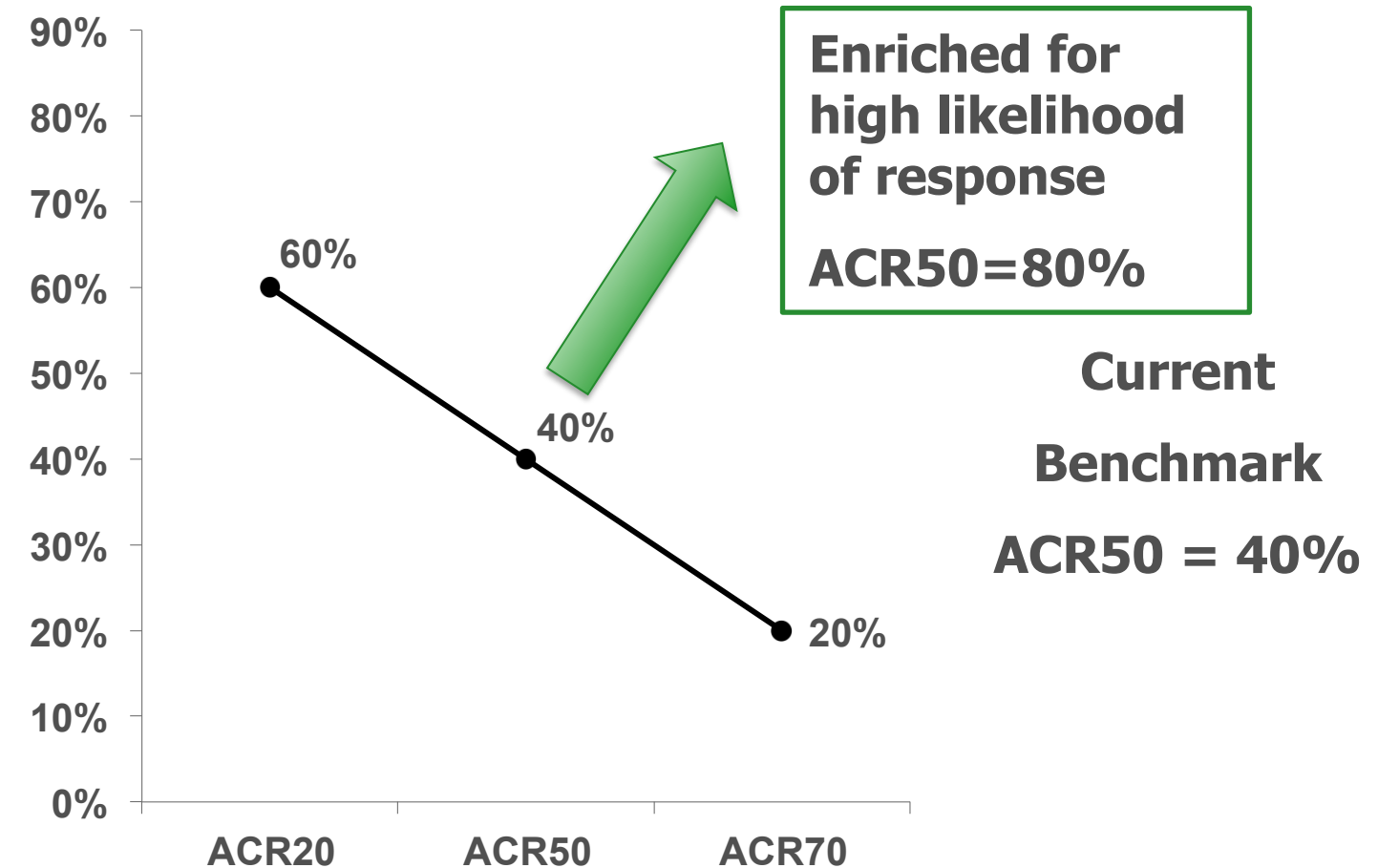
Genome Sequencing and Molecular Profiling



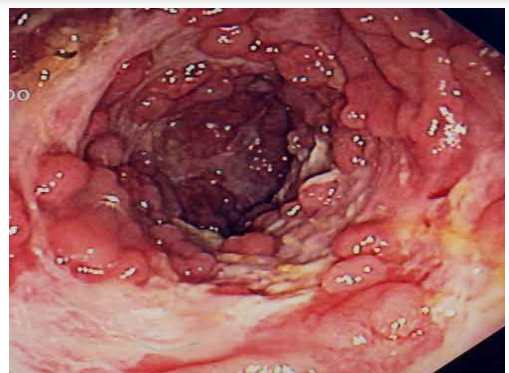
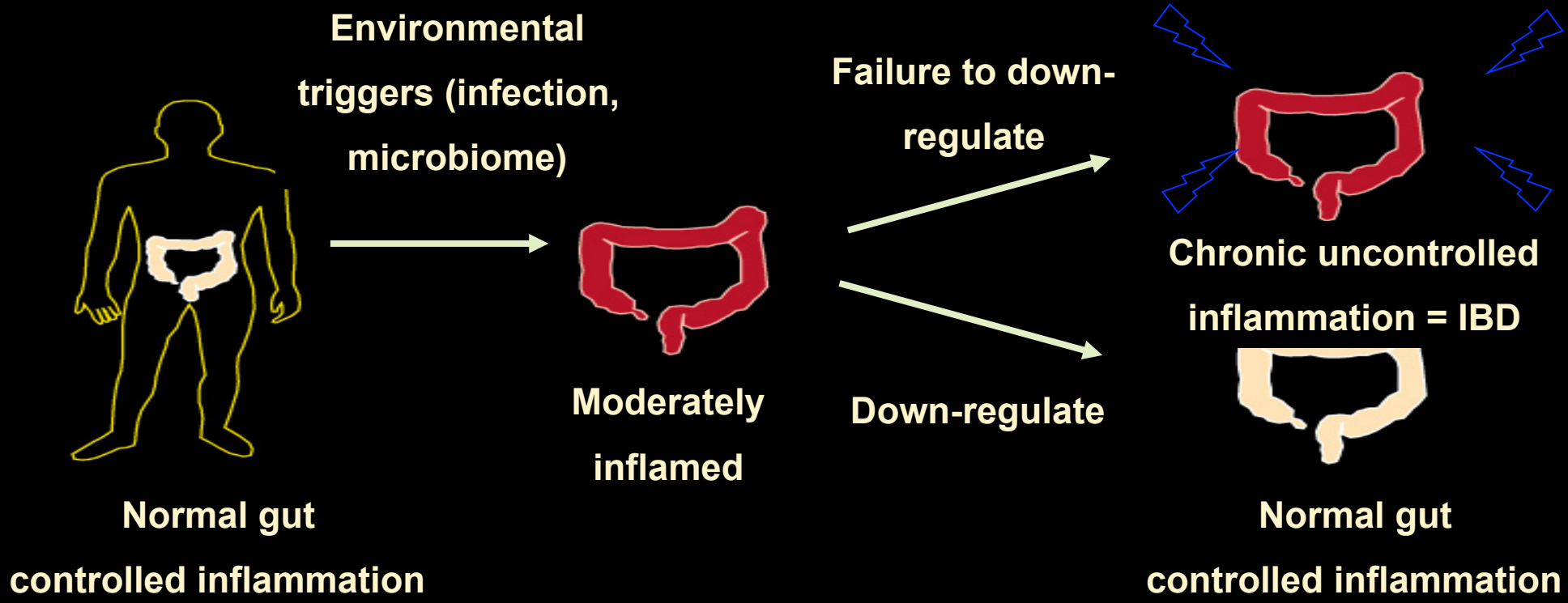
Biomarkers and Personalized Medicine in Rheumatoid Arthritis

Discovering new Solutions for RA Patients

- BATTER-UP consortia for anti-TNF responses in RA
- Whole genome sequencing of RA patients



Inflammatory Bowel Disease (IBD): Crohn's Disease and Ulcerative Colitis



Deep Ulceration



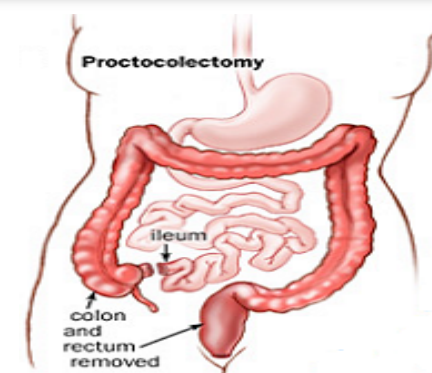
Stricture



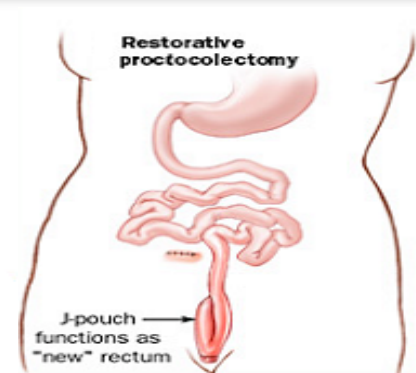
Perianal Fistula



Anterior Uveitis

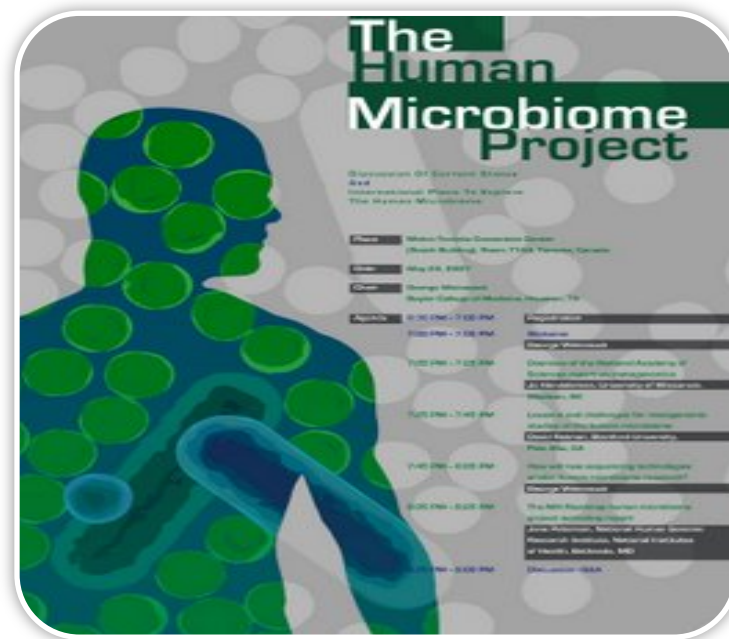
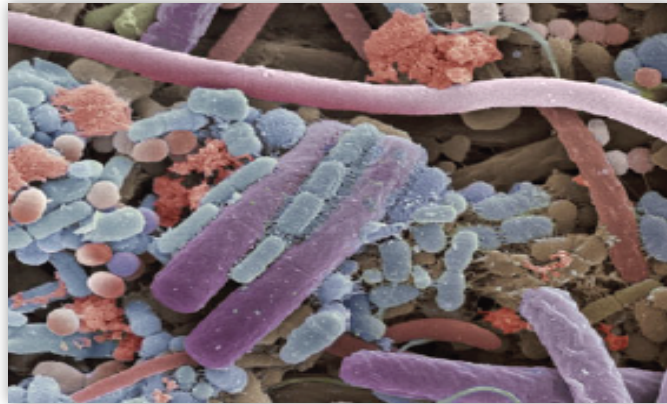


Proctocolectomy



Profiling the Microbiome

Defining New Solutions for IBD Patients

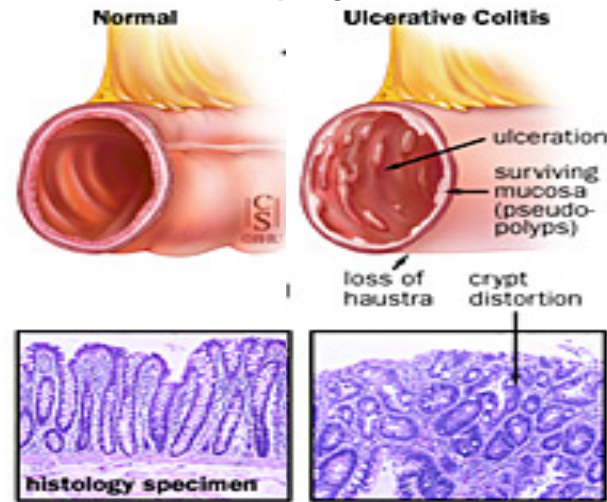


- The gut, largest immune organ in the body
- Dysfunctional microbiome-host interactions in IBD
- Microbiome profiling initiatives:
 - Second Genome
 - Janssen clinical trials
 - Microbiota Sequencing
 - Informatics
 - Microbial biology
 - Immunology

Companion-Dx for Anti-TNF Treatment in UC

Discovering New Solutions for IBD Patients

Tissue Biopsy collections



Personalized Medicine
Response Prediction



- Gene expression profiling of tissue biopsies in ulcerative colitis (UC) in REMICADE[®] and SIMPONI[®] trials
- Identified predictor of response to anti-TNF treatment for personalized medicine
- Prospective validation trial underway

Toedter G, Li K, Marano C, et al. Gene Expression Profiling and Response Signatures Associated With Differential Responses to Infliximab Treatment in Ulcerative Colitis. *Am J Gastroenterol* 2011; 106:1272–1280.

Genomics Impact on Pharma R&D

- Unprecedented opportunity to understand disease and create new medicines/solutions
- To fully apply genomic information to drug development we need:
 - Bioinformatics, computing and network pharmacology expertise to translate “big data” into knowledge
 - Cross disciplinary training programs
 - New business models; public/private consortia
 - Clear regulatory guidelines

“The patients are waiting!”



Dr. Paul Janssen

janssen

PHARMACEUTICAL COMPANIES

OF *Johnson & Johnson*

