SAPIEN BIOSCIENCES

Bio-Bank

Diagnostics and Biomarkers
Assay development and commercialization

Research & Clinical Support Services

A joint venture with

Apollo HOSPITALS
TOUCHING LIVES

The ‘Essence’ of Sapien

India’s 1st commercial **Bio-bank** with systematic archive of ethically consented, anonymized patient samples & associated data

With a mandate to utilize these samples to revolutionize healthcare scenario by contributing to drug discovery, novel diagnostics, biomarkers, personalized medicine alike…

To ensure effective clinical outcome !!

Sapien is not a vendor of samples.
Banked samples are used only for R&D
NOT FOR regenerative medicine or transplantation

Leadership team

Sreevatsa Natarajan
CEO

- Experienced business professional with over 16 yrs of global pharma experience in drug discovery, clinical research, portfolio mgt, licensing & bus. dev.
- Extensive experience in constructing & negotiating several collaboration & licensing deals and managing global alliances.
- Proven track record of leadership roles across several global drug discovery organizations & business models
- Participated in and managed teams that have developed and registered several NCEs (Oxycontin, Telaprevir etc)

Jugnu Jain, Ph.D.
CSO

- Molecular and cell biologist experienced in the use of primary human samples & related cellular paradigms for drug discovery & target validation
- PhD in Genetics (Cambridge), post-doc in immunology (Harvard) with 25 years of post-PhD experience in autoimmune, inflammation & neuro-inflammation, cancer & diabetes therapeutic areas.
- Led biology teams on novel drug discovery targets & contributed to IND filing for many molecules.
- Extensive R&D leadership experience and proven track record of forging several successful R&D collaborations

Leadership team

- **Dr Lakshmipathi Khandrika** – Senior Scientist - Over 14 years of experience in Molecular Biology and ~8 years in Cancer Cell Biology (India, US, Europe).
- **Dr Mukesh Gandhari** – Principal Scientist – over 9 years of experience in drug discovery and biopharmaceuticals at Sun Pharmaceuticals, GVK Biosciences
- **Dr. Prasanna Kumar** – Associate director – Strategic marketing Clinical diagnostics - Physician with about 7 years of ICU and ER experience, MBA + 4 Yrs of Pharma diagnostics experience in Elli Lilly , MedGenome.
- **Dr. Rachna Goyal** – Associate Director – Business and project management – Trained cell Biologist with over 9 years of customer facing project management experience at Millipore, Vimta, Lonza
- **Dr. Soma Chatterjee** – Associate director – Biobank operations – Trained cancer biologist with over 9 years of experience in ethical tissue sourcing and cell biology applications at Lonza
- **Dr. Sumeda Dange** – Quality Assurance – Trained Pharmacist with PhD in Electro-physiology. Decade of Industrial exposure in the field of Quality Assurance at Dr. Reddy's and Nektar Therapeutics

The Apollo advantage

The Apollo set-up – Asia's largest hospital network

Owned	Managed	Total		Owned	Managed	Total
6,684	1,933	8,617	across	39	11	50

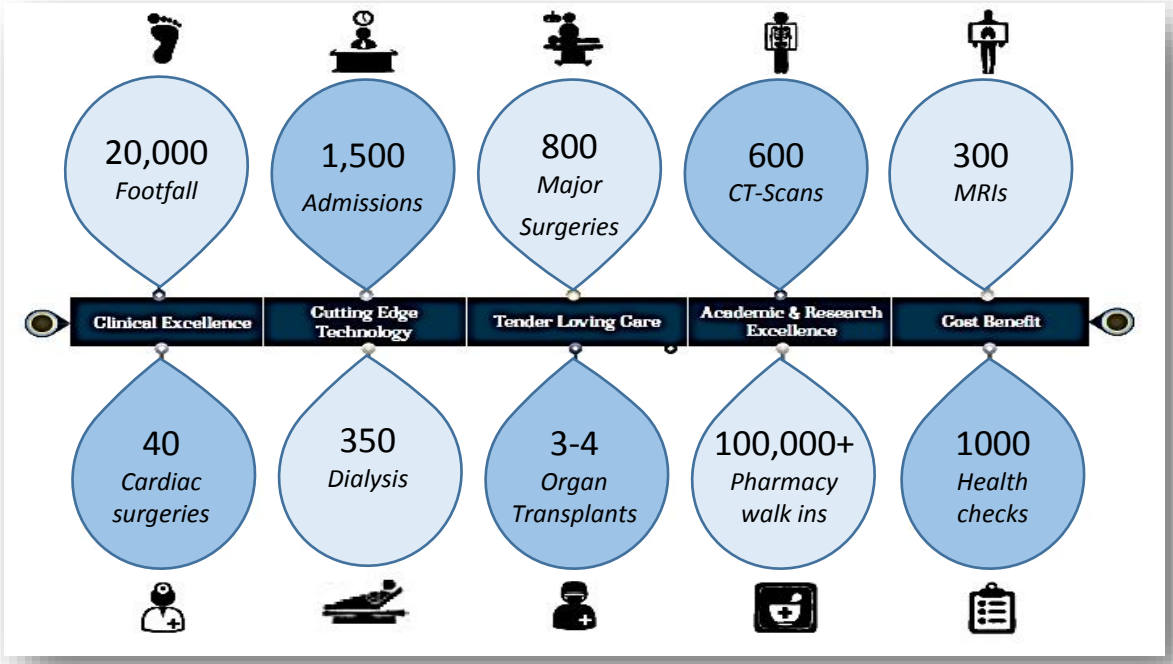
Tertiary, Super Specialty & Secondary Care

JCI accreditation 8 | NABH accreditation 10

Employed + "fee for service" Doctors	Nurses	Paramedics
5,870	9,469	3,141

67% of Consolidated Revenues

A typical weekday in the world of Apollo



FY14 at Apollo hospitals

325,000+ Admissions	3,000,000 Out-Patients	250,000+ Preventive Health Checks
10,000 Heart Surgeries	5,000+ Joint Replacements	13,000 Neuro Surgical Operations
500 Robotic Surgeries	1,000+ Kidney Transplants	375 Liver Transplants
120 Countries Medical Value Travel	150 Bone Marrow Transplants	150,000+ Radiotherapy Sessions 42,000+ Chemotherapy Sittings

An abundant resource of diseased tissue samples and an honest will to use them for betterment of mankind

- contributing to diagnostics and drug development
- offering these new drugs / diagnostics for their patients

Our win-win collaboration to revolutionize healthcare

Sapien has Exclusive access to ethically banked clinical tissue samples and KOLs @ Apollo

To utilize for in-house and collaborative R&D

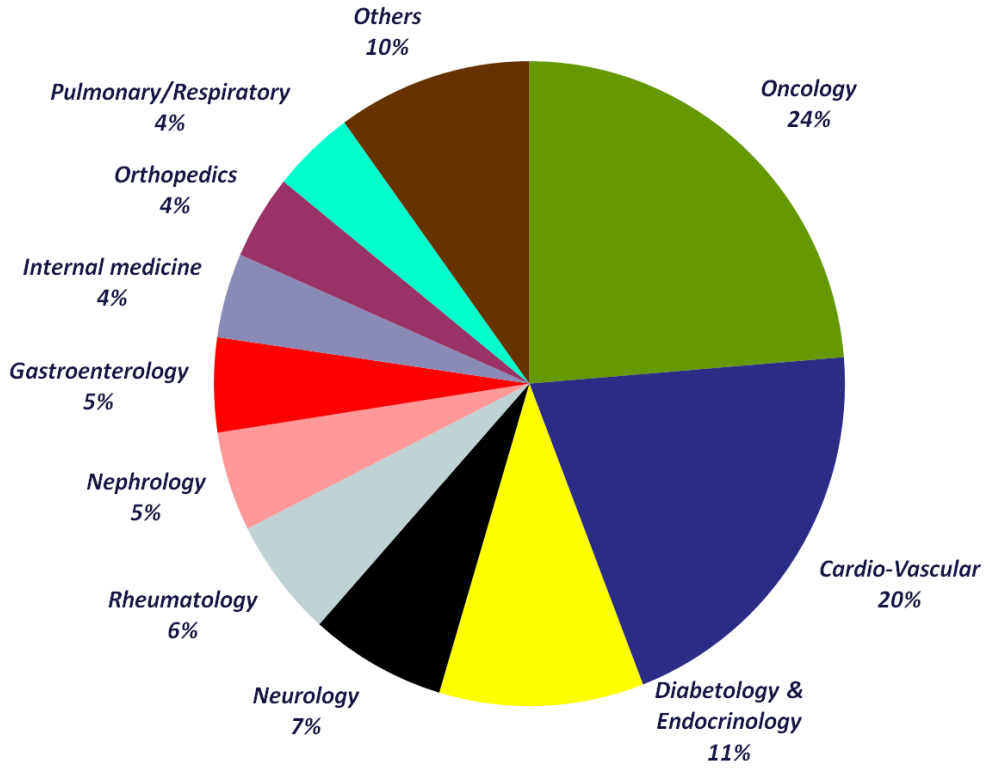
Sapien is an Exclusive front end for introducing cutting edge diagnostics at Apollo network

Developed in-house or by collaborators

Access to clinical network: Apollo Research and Innovation

- Cumulative experience of over 800 trials with 70% of these for FDA or EU registration
- Potential to undertake more than 200 trials at any given time

Reach	Resources	Processes
17 networked sites	60 GCP trained CR Coordinators	Standardized SOPs
54 Apollo Hospitals	200 GCP trained PIs	Clinical Trials Management System(CTMS)
72 Apollo Clinics	Over 100 clinicians willing to participate	Highly Vigilant Ethics Committees



Current trials across therapeutic areas

Some operational insight

Sample types banked at Sapien

- **Retrospective – after anonymization.**
  - FFPE blocks – Tumor as well as adjacent non-tumor
- **Prospective samples - with informed consent**
  - Fresh tumor and adjacent non-tumor samples
  - Hematological tumors: Cell types (PBMCs, T/B cells, platelets etc.)
  - Blood, Plasma, Serum
  - Saliva, Urine, BAL, Pleural fluid, synovial fluid etc.
  - *Non-diseased specimens*
- **Health Check-up left over samples - with informed consent**
  - Serum / Blood / Urine - With extremely rich associated data

~50,000 patients' blocks & data are being retrieved at Hyd. Expect ~5 lakh samples in 5 years across Apollo network

Ethics of Bio-banking – Peace of mind for researchers

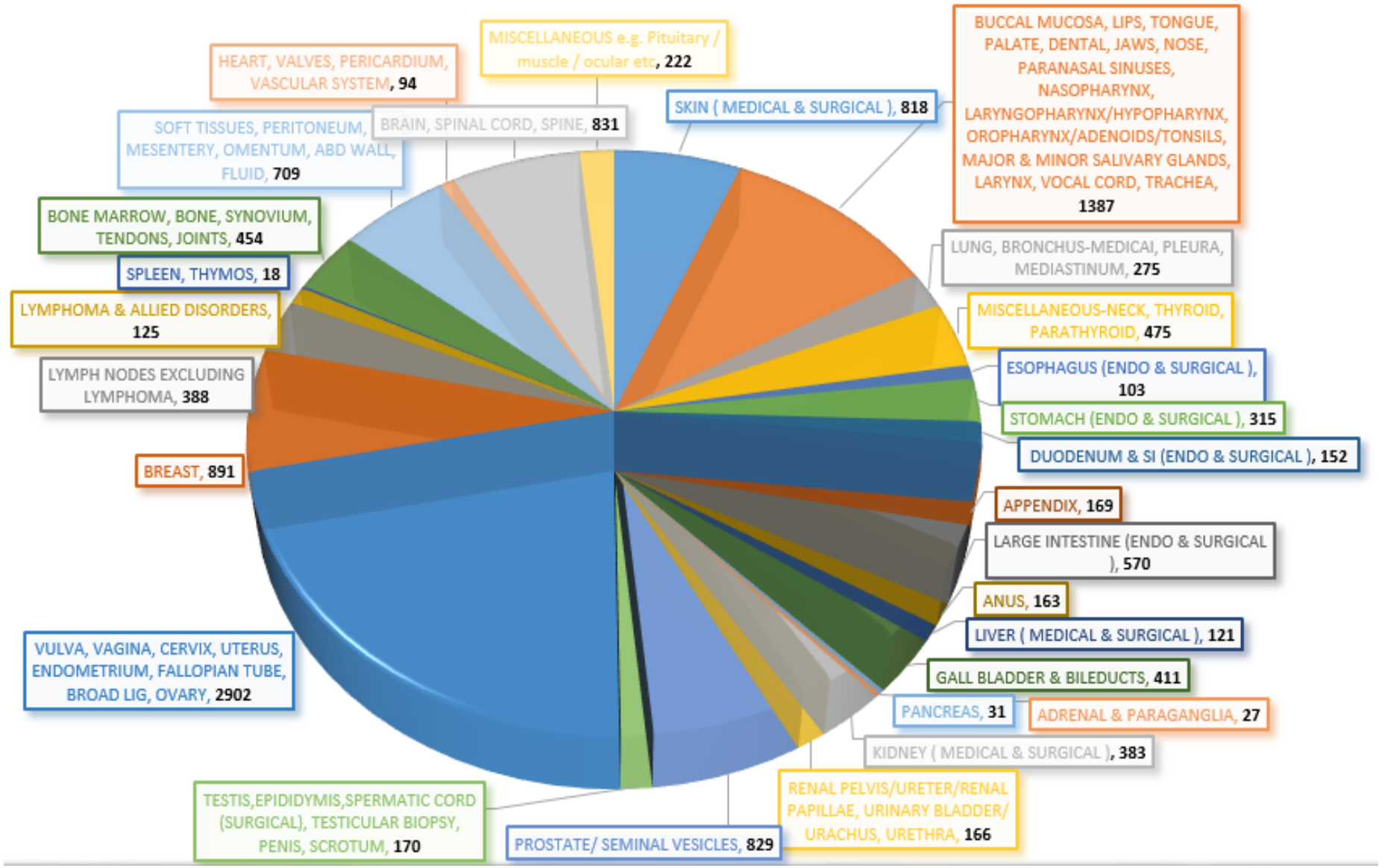
- Sapien works within ICMR and international guidelines, and follows high ethical norms with respect to transparency and patient privacy
- Sapien banks samples after Hospital EC approval & with Informed Consent
  - Informed consent form language follows ICMR guidelines
  - Retrospective samples (FFPE blocks) after anonymization
  - Prospective samples with ICF
- Sapien's Repository Ethics Committee (REC) also being constituted to review projects internally

Access to fresh tissues @ Sapien

- Accessibility across Apollo network - Possible to source many more sample types based on requirement !!
- **Many of these have been cultured to derive primary cancer cells e.g. breast / prostate/ Glioma**

Fresh tissues @ Sapien - Currently banked / feasible to source				
Abdominal cavity	Tonsil	Parathyroid	Malignant Lymph nodes	Surgical resection of Adenoids
Bladder	Glossectomy	Parotid	Laryngectomy	Surgical resection of the spleen
Brain	Thyroid	Pancreas	Uterus	Surgical resection of Tonsils
Breast	Testis	Ovary	Prostate	Fibroids from uterus
Kidney	Stomach	Omentum	Penis	Spinal Tumor
Colon	Spleen	Oesophagus	Normal Lymph nodes	Liposuction
Buccal Mucosa	Spinal Cord	Lung	Male normal breast reduction	Vitreous gel from eye
Gluteal Region	Rectum	Liver	Female normal Breast reduction	Synovial fluid
Cervix			Non malignant hysterectomy sample	Cord Blood

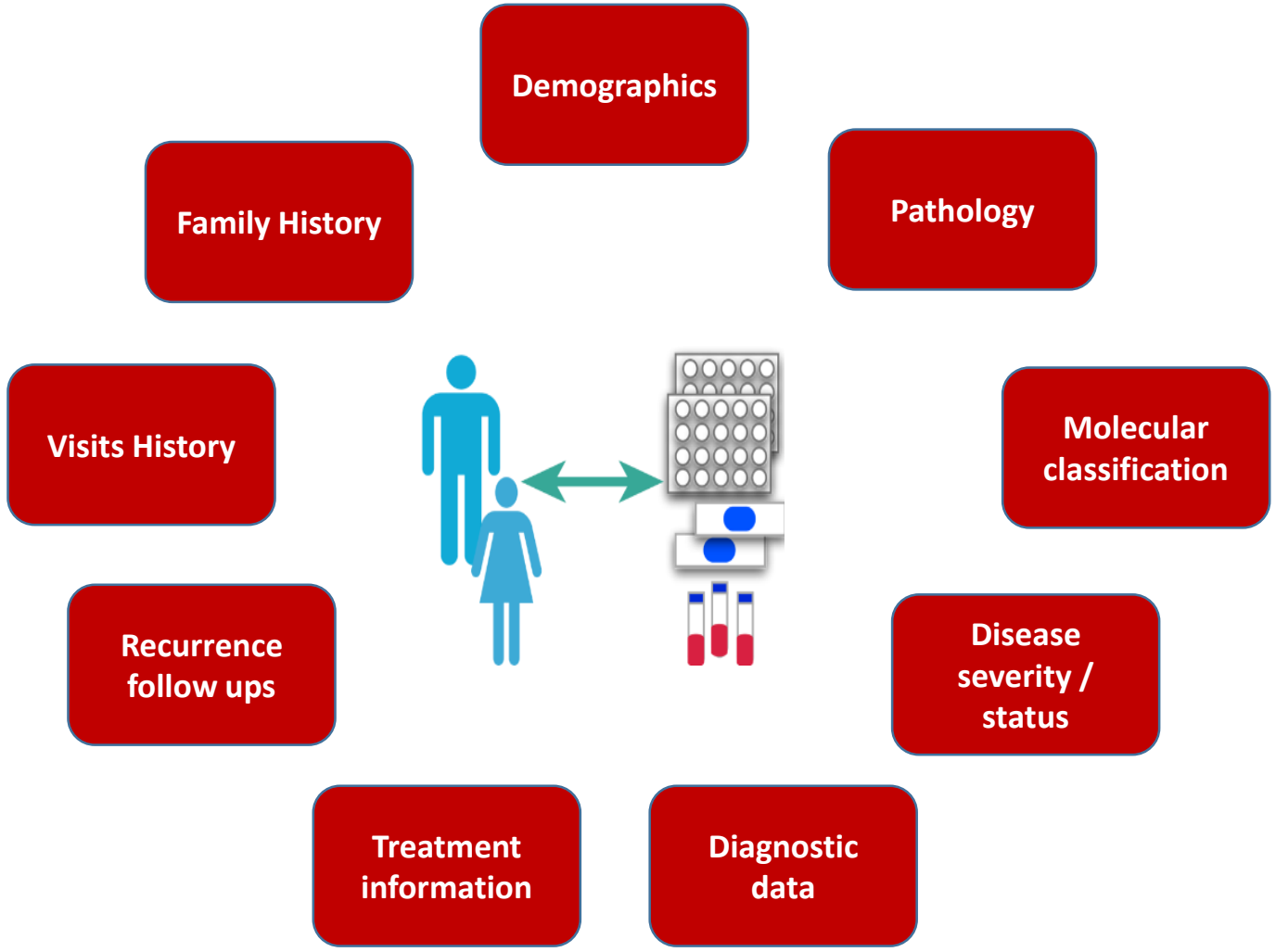
Current inventory of FFPE Blocks – source tissue wise



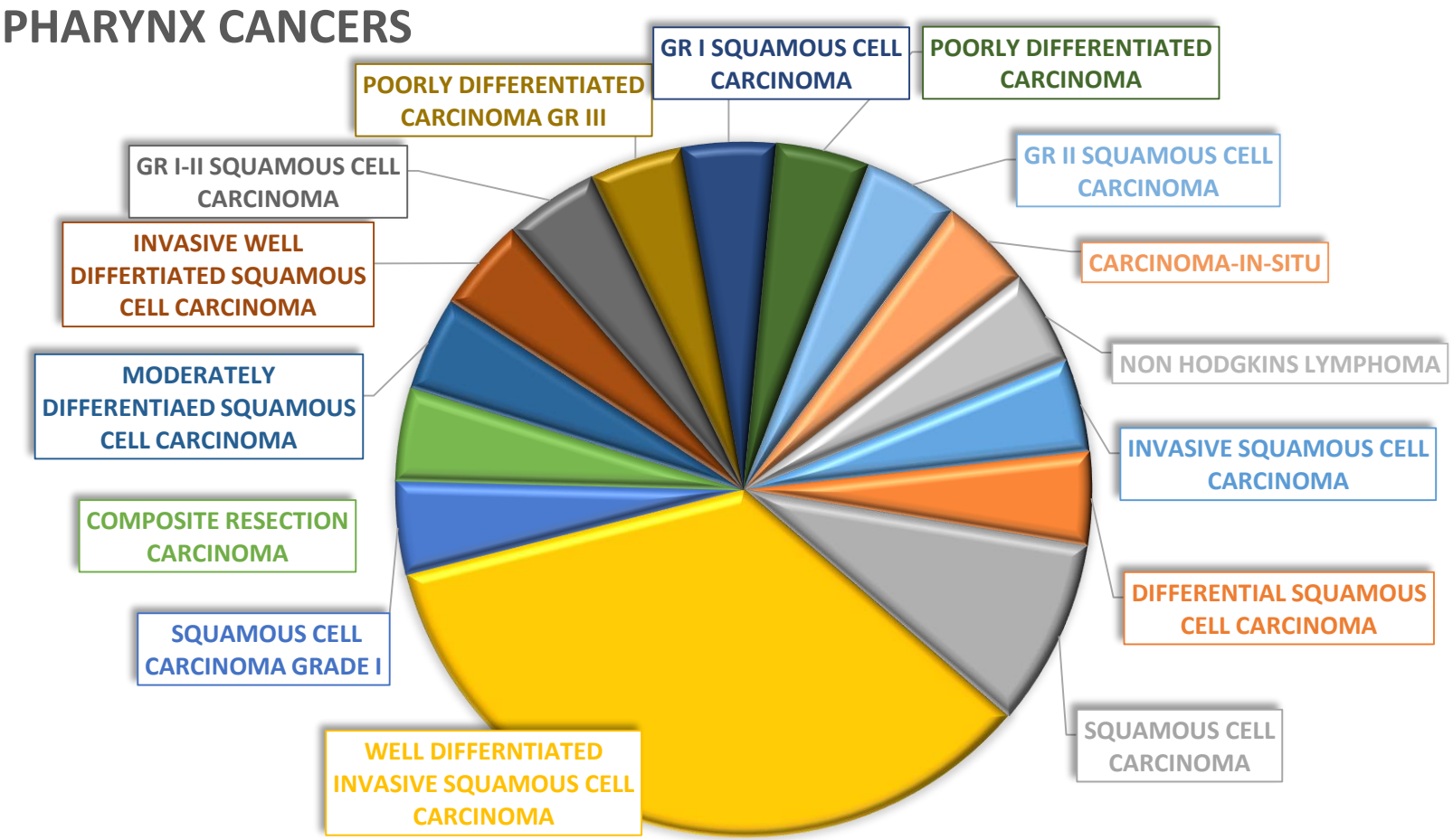
* Data from single location - Apollo Hyderabad for 3 yrs. Sapien is working on systematically archiving samples from across Apollo network over several years

Associated information: holds promise for future

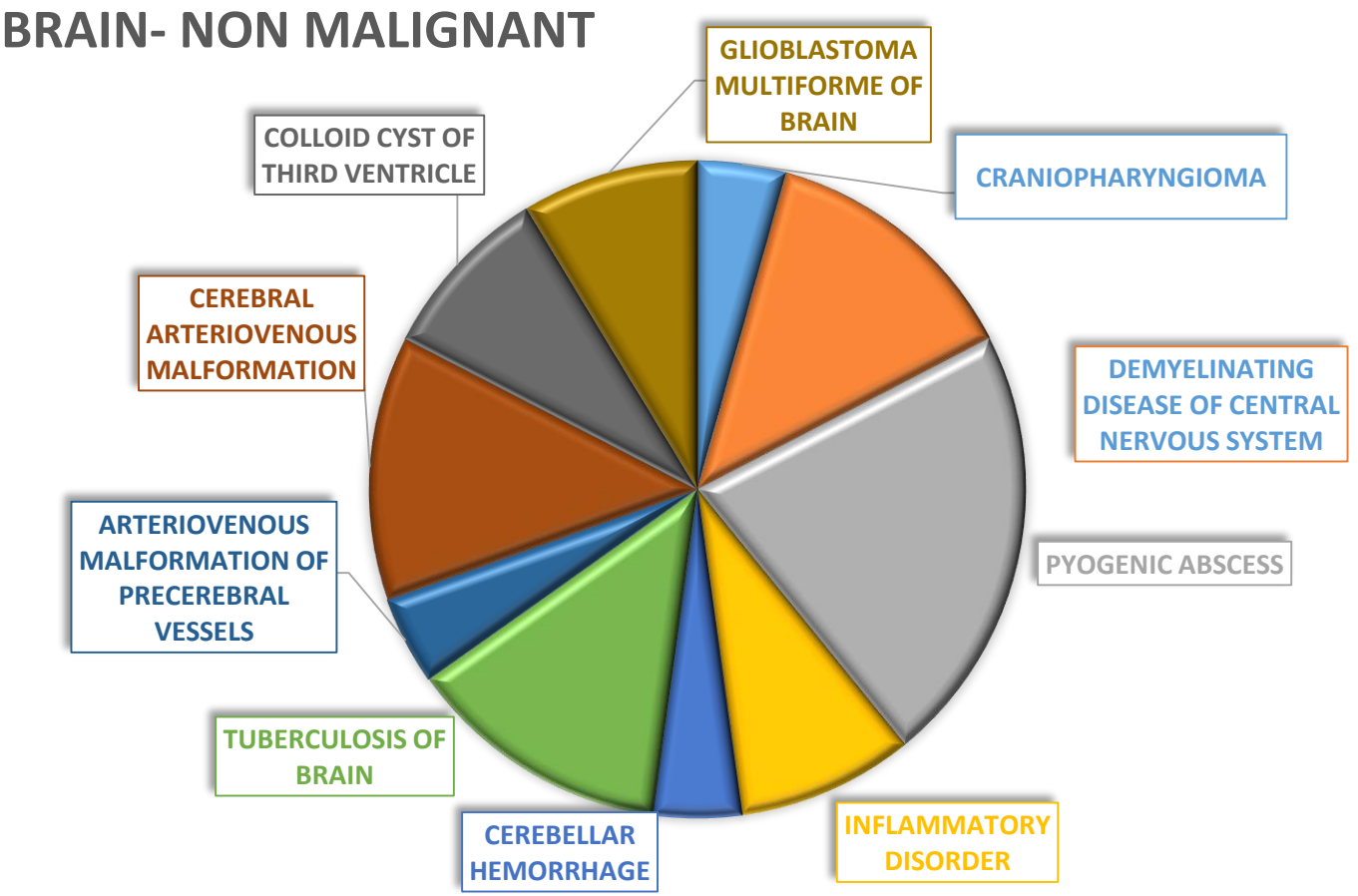
Any specific inclusion / exclusion criteria can be set as per need of study



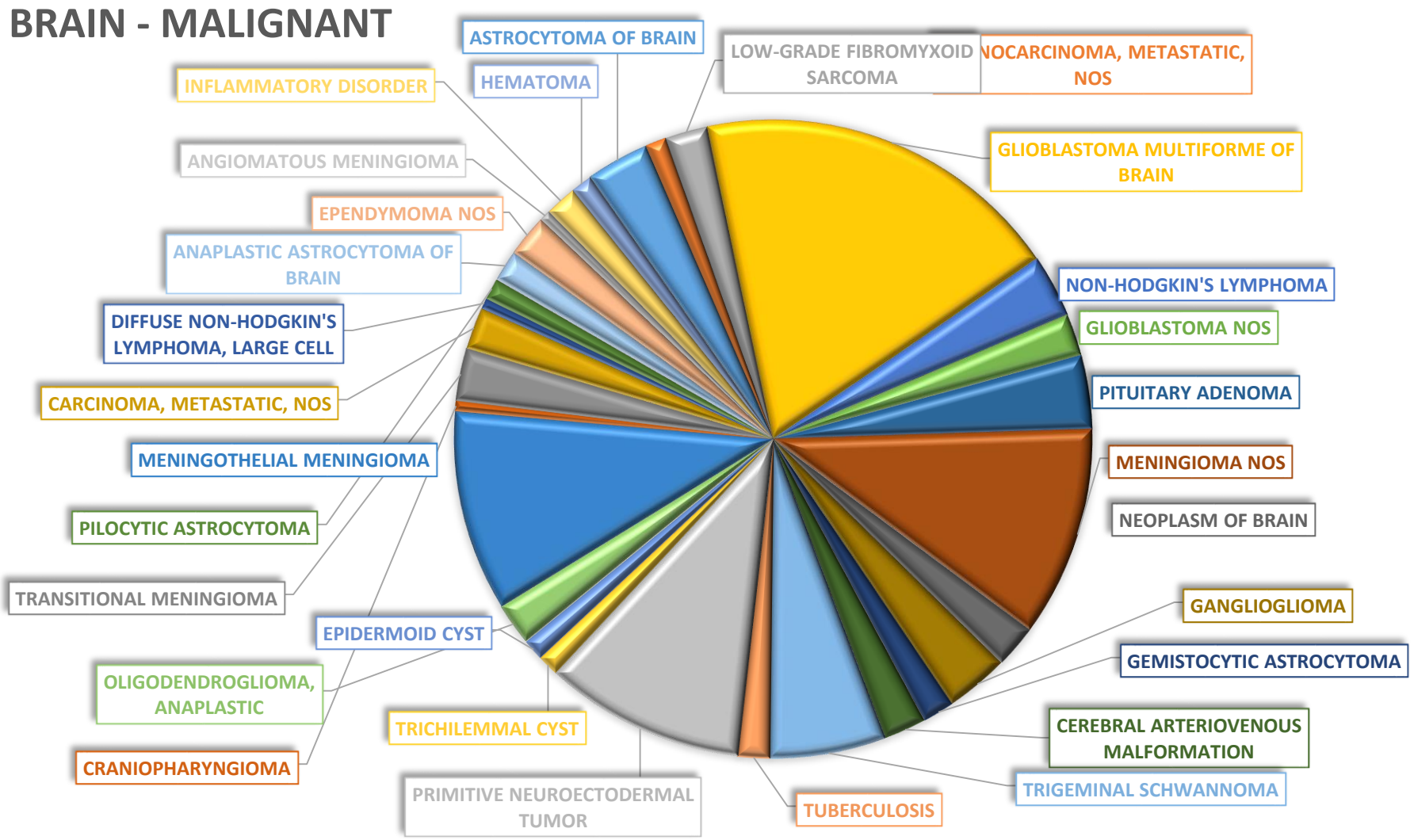
Sneak peek into the diversity of banked samples



Sneak peek into the diversity of banked samples

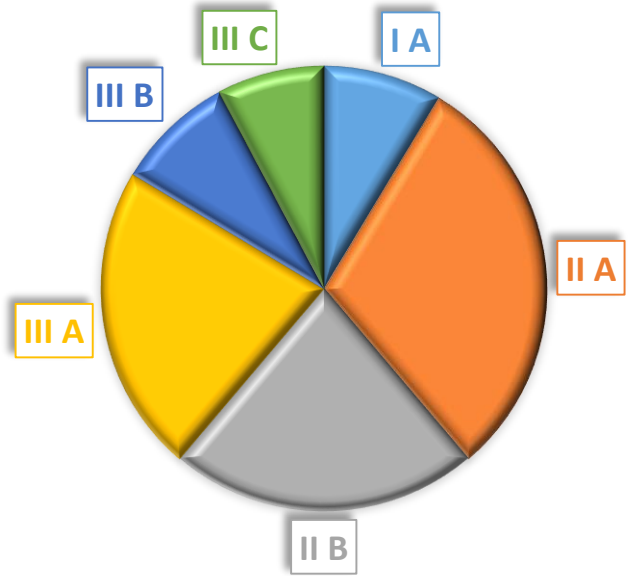


Sneak peek into the diversity of banked samples

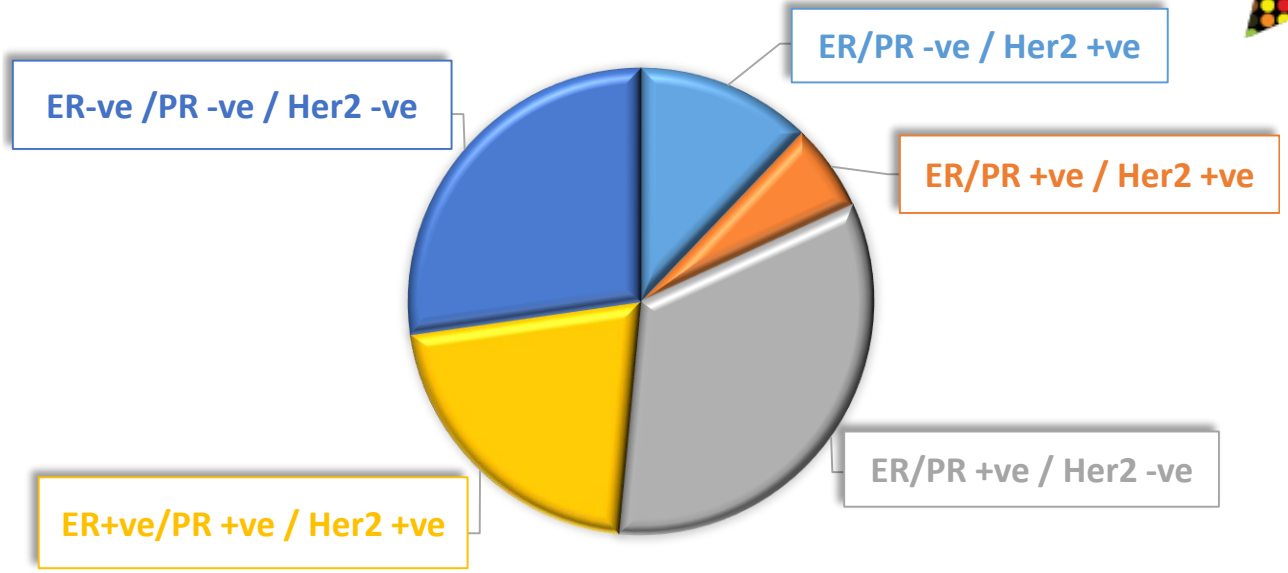


Sneak peek into the diversity of banked samples

BREAST CANCER - STAGES



BREAST CANCER - ER/PR/Her2 STATUS*



* Information only for a subset of the entire sample inventory

Sneak peek into the associated information*

Sample Information				
Serial No.	Date & method of diagnosis	Date of birth, Age at diagnosis, Sex	Registration / hospital #	Pathology block #/ Slide #
ABC001	14th July 2005, lumpectomy	01-12-1960; 45/F	XYZ1234	5124/05

Pathological information				
Specimen type: MRM/BCS surgery with date	DCIS/IDC/ILC /Papillary carcinoma & Grade	TNM & stage, Metastasis at detection	ER/PR/Her-2 /Ki67/P53	Miscelleneous:, FISH for Her-2/neu Oncotype Dx score
BCS; 21st July 2005	IDC-3 with DCIS focus	pT2N2M0, Stage 2	70%P/45%P/ 1+/60%/Not done	FISH: negative; ODx score: 18

Chemotherapy information		
Neo-adjuvant/ Adjuvant, Drugs/Regimen and # of cycles	Dates of CT	Repeat CT with drugs and dates
Adjuvant, FACx4 + Paclitaxelx12 ;	September 2005-March 2006	Capecitabine x6 in January 2007-March 2007

Radiotherapy information		
RT: Type, Dose and fractions	Dates of RT given	Miscelleneous: Booster dose ?
EBRT; 58 Gy/28 Fractions	April 2006-May 2006	10Gy/5 Fractions June 2006

Hormonal therapy		
Neo-adjuvant/ Adjuvant & Drug name	Dose & dates of HT taken	If HT changed, new drug name & date
Adjuvant, Tamoxifen 20mg/day	Started July 2006 for 5 yrs	Chaged to AI July 2011

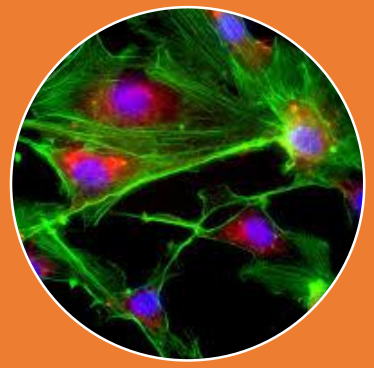
Recurrence information	
Date & site of recurrence	How was recurrence detected?
December 2006, Liver and Bone	PET-CT and Bone scan

Current Status			
Last F/up date	Alive: Date & With mets or not	Passed away: Cause of death & date	Miscelleneous:
12th Sept 2013	Alive with liver & bone mets	N/A	On regular f/up, every 3 months; no more new mets as assessed by CxR, US(A+P), PET-CT,

Example of associated data for Breast cancer samples

* that can be collated and provided based on requirement.

R&D Infrastructure available to Sapien



Flow cytometry

Cell sorting

Fluorescent microscopy

Laser scanning confocal

SNPs, SNP arrays

Sequencing

Bioinformatics including pathway/ systems biology

Biacore

HPLC

GCMS

LC-MALDI-TOF

X-Ray diffraction

CD

Karyotyping

FISH

ISH

ELISAs

In-house @ Sapien / Apollo or at strategic collaborators

Sapien's Pipeline of PM Tests/Diagnostics

- **Personal Genomics** (Preventive Health Check Context - Physician Support)
  - **Prognostic Tests** (Disease Risk Assessment)
    - **Asymptomatic Patient**
      - Tests covering multiple diseases
        - myCarDiO
        - Multi-Disease Panels
    - **Symptomatic patient or known family history of disease**
      - Disease Specific Panels
        - Oncology
        - Cardiovasc.
        - Neurology
        - Gynaec
        - Lung Cancer & Nicotine Dependence
        - Diet & Fitness
- **Clinical Genomics** (Clinical context – Physician Prescription)
  - **Diagnostic Tests** (Differential Disease Diagnosis)
    - Rare Genetic Dis
    - Hereditary Cancers
    - Somatic Cancers
    - Eye Diseases
    - Cardiovascular
    - Diabetes (MODY)
    - Autism
    - Cystic Fibrosis
    - Muscular Dystrophy
    - Peri-natal Genetics & Proteomics
    - Single Gene Tests
    - Non-Invasive Pre-natal Test for Trisomies
  - **Theranostic Tests** (Tx Monitoring/Optimization)
    - PGx panels
      - Oncology
      - Diabetes
      - Cardiovasc.
      - Neurology
      - Anti-Virals
      - Inflammation
    - CTC Test
    - CEC Test
    - myPLATELET
    - Breast Cancer Recurrence

Sapien projects

In sourced tests

Some case studies

Case study @ Sapien:

*my*PLATELET™ – Enabling Tailored Anti-Platelet Therapy

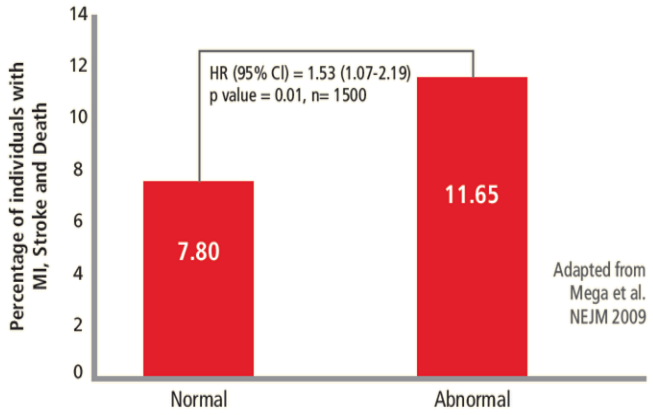
- Proprietary combo test & analytical paradigm enables physicians to make optimal drug & dose adjustments to personalize ANTI PLATELET THERAPY.
- Test fully validated & currently in use at Apollo and some other hospitals in Hyderabad

Case study @ Sapien:

*my*PLATELET™ – Rationale for Combo test

- CYP2C19 gene variants affect bioavailability of clopidogrel compromising its anti-platelet activity.
- Patients with these genetic variants are at higher risk of major cardiovascular events, such as heart attack, stroke and death, despite being on anti-platelet therapy.

Increased risk associated with primary efficacy outcome in PCI patients that are carriers of CYP2C19 reduced function alleles (*2, *3)

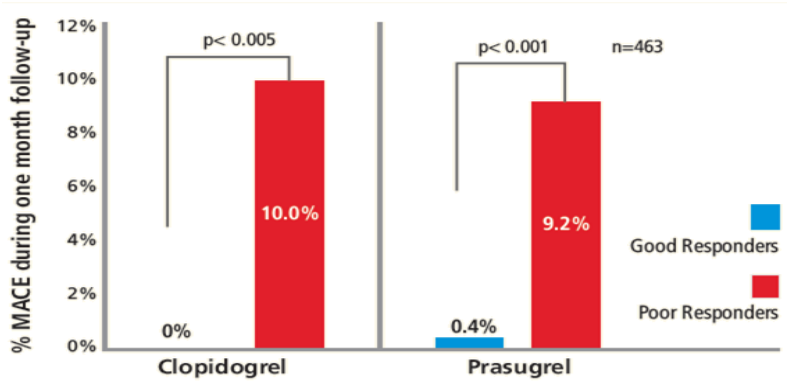


CYP2C19 Gene Variants Affect Clopidogrel Activity

Platelet Reactivity Assay can Benefit PCI-Stent Patients

- PR assay estimates functional response of platelets to clopidogrel, prasugrel & ticagrelor
- Studies have demonstrated a significant correlation between the PR Assay-guided treatment and reduction in Major Adverse Cardiovascular Events (MACE), especially in PCI patients and patients with recurrent ischemic events

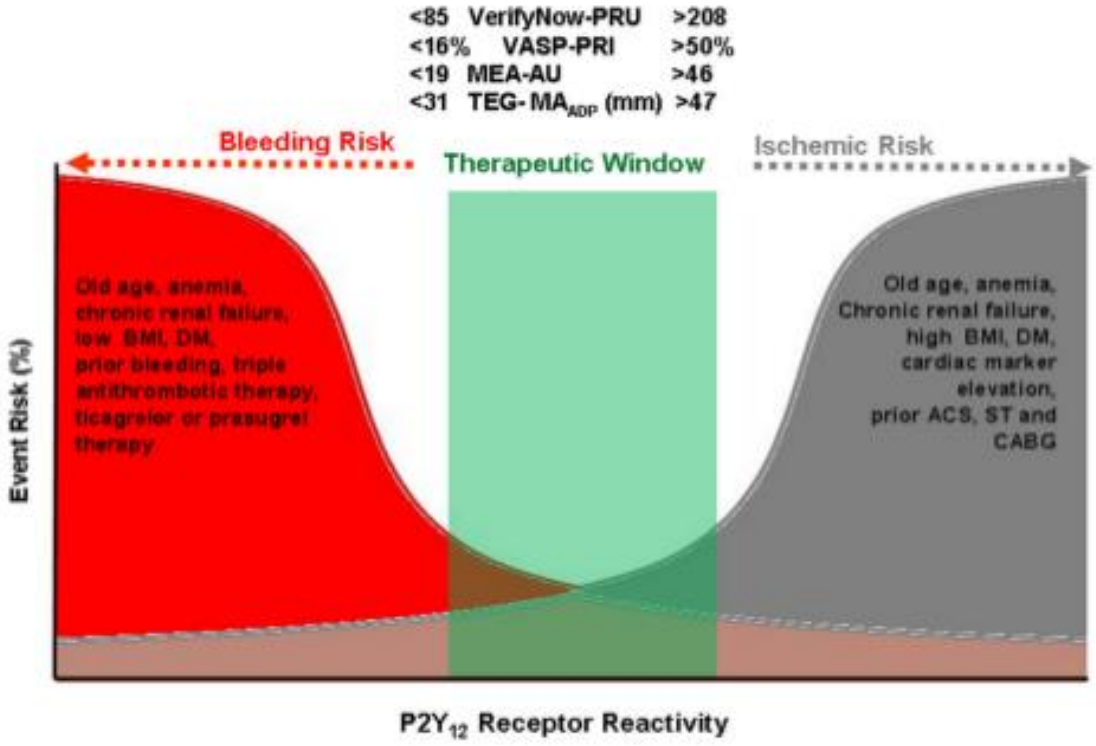
Significant reduction in MACE in good responders as determined by PR assay

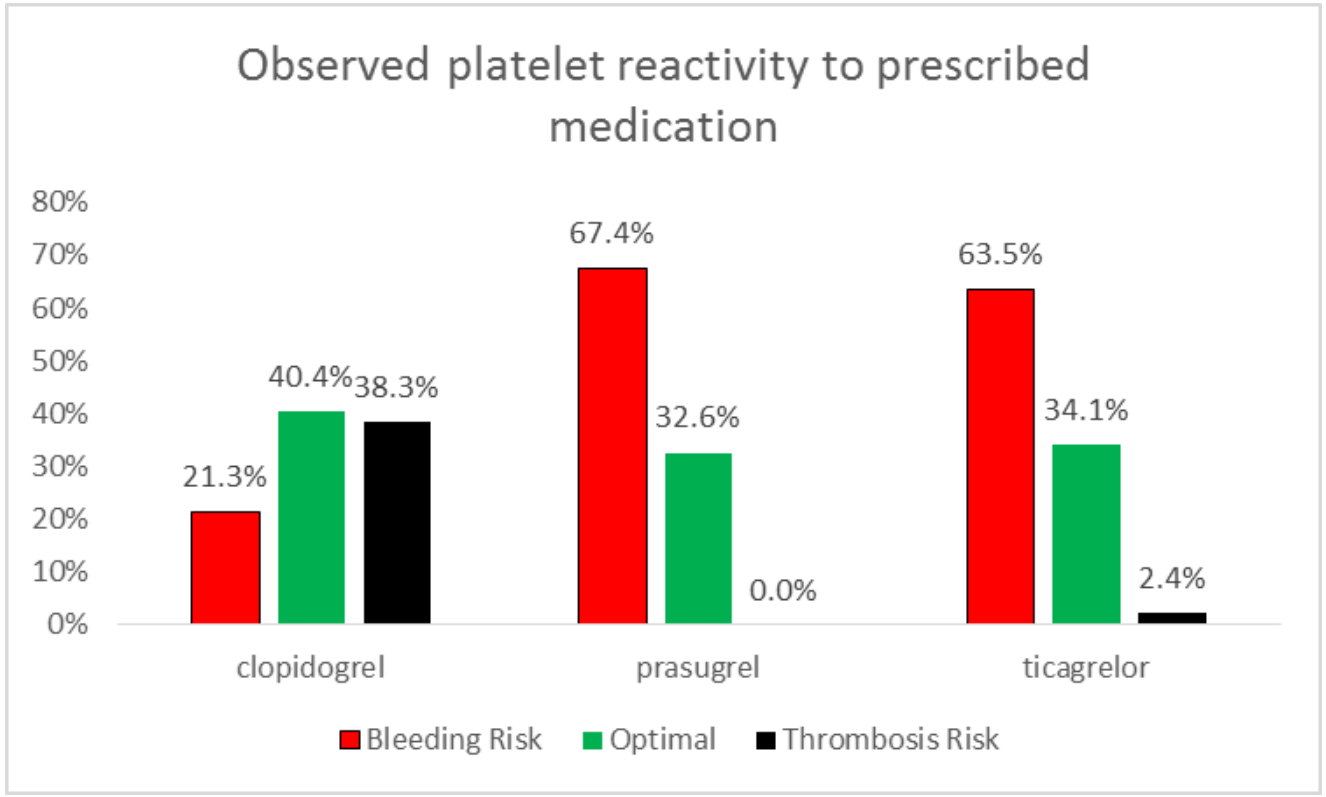


Case study @ Sapien:

*my*PLATELET™ – Enabling Tailored Anti-Platelet Therapy

Sapien data: Majority of Indian PCI patients are not in optimal PR window for any of the 3 drugs when tested initially





Consensus paper from Group on On-Treatment Platelet Reactivity, Tantry et al, JACC 2013: 62: 2261

Case study @ Sapien:

*my*PLATELET™ – Impact – Actionable results for 76% patients

More than 200 tests performed making a difference in patient therapy for more than 152 patients

Observation / Action	Percentage of patients
Patients that were recommended change in therapy / dosage using myPLATELET Test	**76**
change in drug or dosage was recommended for either efficacy or safety reasons using genotype and PFT	53
Increased monitoring was recommended due to increased risk of bleeding for patients that could not be switched to clopidogrel	13
Based on genotype, switching from the current more expensive medicine to clopidogrel was feasible thereby providing economic benefit to patient	12

Case Study @ Sapien

*my*CarDiO™ – Enabling Personalized Genetic Risk Assessment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Advancing Science, Personalizing Medicine

Apollo HOSPITALS
TOUCHING LIVES

myCarDiO™
Cardiovascular
Diabetes
Obesity

Personalised Genetic Risk Assessment Report

Patient Information
Name: K. Reddy
Gender: Male
ID: SB.456
DOB: 23.07.1965
Date Collected: 07.06.2014
Date Reported: 21.06.2014

Requesting Physician/Institution
Name: Dr. V. Prasad
Hospital: Apollo Hospitals (Chennai)

his test report is not meant for diagnostic purposes.
formation contained in this report does not constitute medical
dvice and is for information only. Please consult your physician
ior to making any modifications to your treatment or lifestyle.
his test has been customised for Apollo Hospitals by Sapien
iosciences and NutraGene.

NutraGene 2014. All rights reserved.

- Nominally priced, novel SNP-based test that enables assessment of genetic predisposition to CVD, diabetes & obesity;
- Integrated with preventive health checks to allow co-interpretation of genetic risks & health check data
- Test includes pre- & post-test counselling & a follow-up physician appointment
- Roll-out across the Apollo network of hospitals & clinics ongoing
- Apollo is a pioneer in preventive health and does over ~5 Lakh health checks annually; Expect 5-10% adoption rate for this test
- Sapien will also bank samples & data from health checks @ Apollo
- **Will enable Sapien to create a database of over 50K genotype-phenotype correlations with outcomes**
- **Sapien expects to monetize this database for mining disease & treatment outcomes, biomarkers, drug responses etc.**

Case study @ Sapien

FFPE samples for Breast cancer recurrence studies

- Breast cancer recurrence diagnostics can help
  - For optimal planning of effective treatment and avoid excessive chemo/ radio therapy associated with severe side effects.
  - prescribing new targeted drugs as required to make therapy more effective
- Sapien is working with an Indian Diagnostics company for validation of a potential proteomic biomarker panel that may potentially be indicative of the extent of aggressiveness of the cancer thereby enabling the prediction of the risk of disease recurrence within the first five years of initial disease diagnosis.
- We are collaborating with them to provide **retrospective FFPE patient samples for upto ~2000 patients who were diagnosed with Stage 1, 2 & 3A breast cancer**.
- **Associated medical data for upto 5 years from the time of diagnosis will also be made available.**
- **Once the test is validated, Sapien will work with the company to commercialize this test across the Apollo network so that patients can be benefitted.**

Opportunities for collaboration

Opportunities of partnering with Sapien

Apollo HOSPITALS
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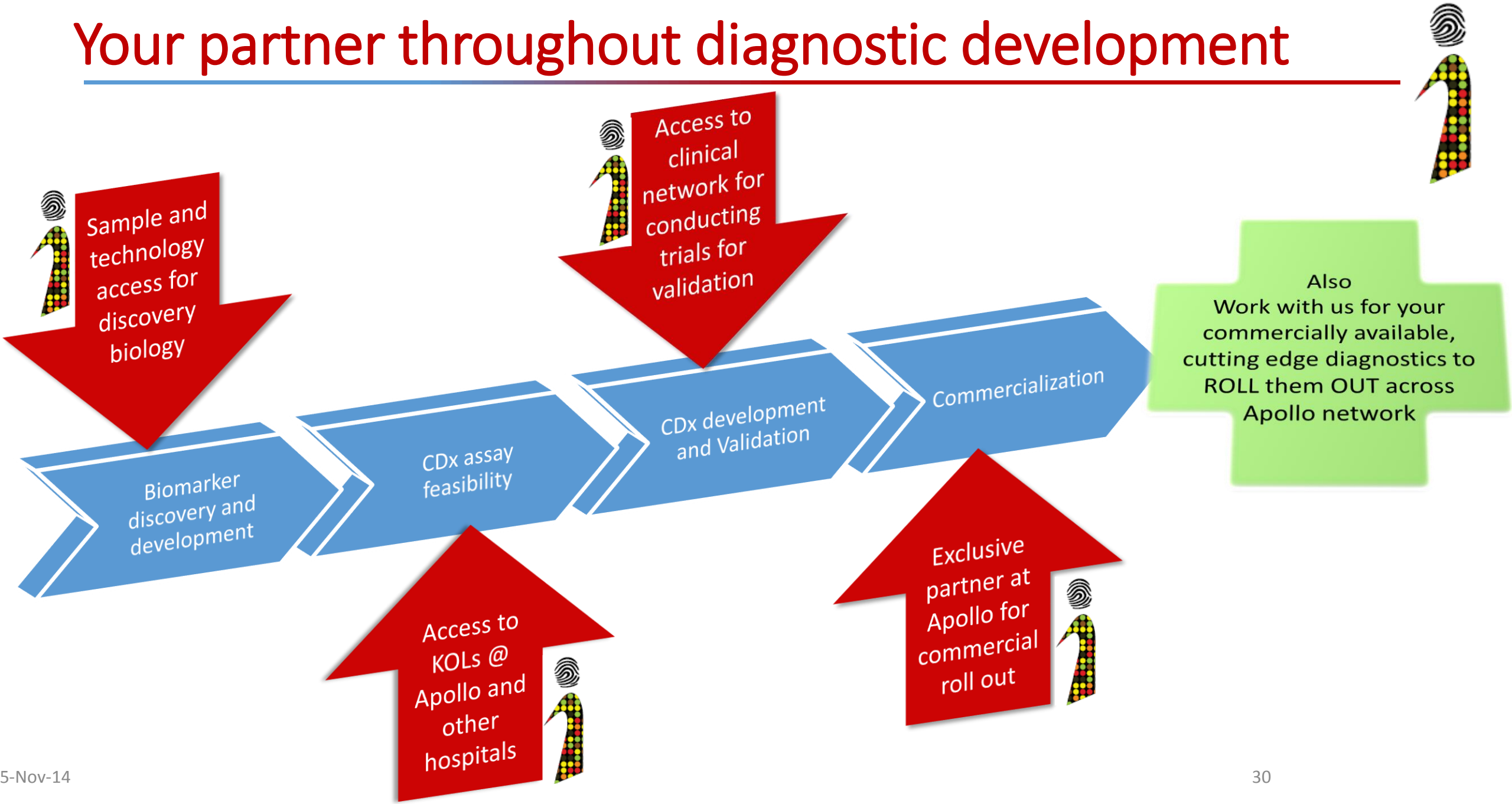
Effective roll out of tests across Apollo network with the available Sapien machinery for BD, marketing, logistics and more

Use the BIOBANK resource along with Sapien's technical expertize to develop assays, Diagnostic tests, identify biomarkers

Access to KOL at Apollo for feedback / beta testing during assay validation

Your organization as a PARTNER for Biomarker discovery/ Diagnostic test development

Your partner throughout diagnostic development



Sapien also works in drug discovery services arena

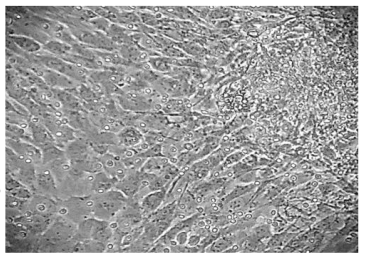
- **Developing Onco*Prime*™ panels utilizing patient derived cancer cells**
  - Screen new chemical or biological entities for companies
  - Generate Indian cancer patient response data by combining *in vitro* assays with outcomes
  - Systematically screen Indian cancers against a 'pill box'
  - Can repurpose drugs / combinations to benefit patients
  - Conduct gene profiling of Indian cancers

ADVANTAGE !! mimics clinical variability in terms of:

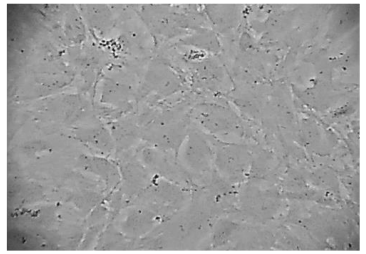
- **Genetic & Disease state based diversity for robust screening**
- **Short term cultures retaining clinically relevant features of the disease (unlike cell lines) including heterogeneity, proliferation rate and gene expression profiles**

Eg. Glioma Panel covering different stages and genetic make-up

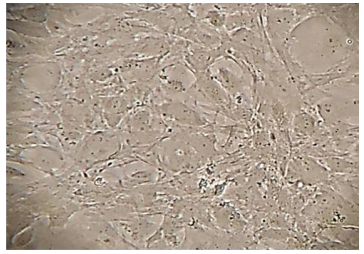
Sample ID	Age	Sex	Pathology
SB-Gm-038	58	M	Glioblastoma Multiforme Gr IV
SB-Gm-085	54	F	Glioblastoma Multiforme Gr IV
SB-Gm-144	38	F	High Grade Glioma
SB-Gm-295	36	F	Anaplastic Astrocytoma Gr III
SB-Gm-298	35	F	Glioblastoma Multiforme Gr IV
SB-Gm-305	58	M	Gemistocytic Astrocytoma Gr II
SB-Gm-474	49	M	Anaplastic Oligodendroglioma Gr III
SB-Gm-5972	44	F	Anaplastic Astrocytoma Gr III



P0 explant 8 day



P2 5 day



P4 5 day

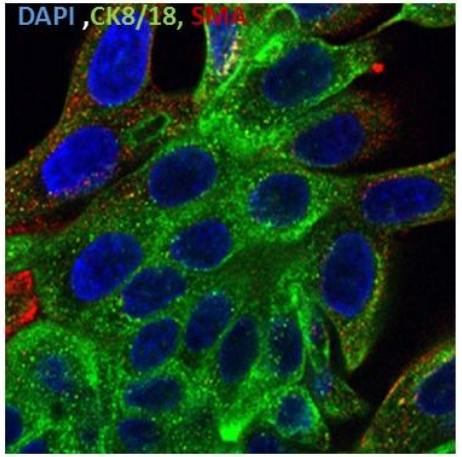
Developing similar panels for Prostate cancer, breast cancer and more..

Sapien also works in drug discovery services arena

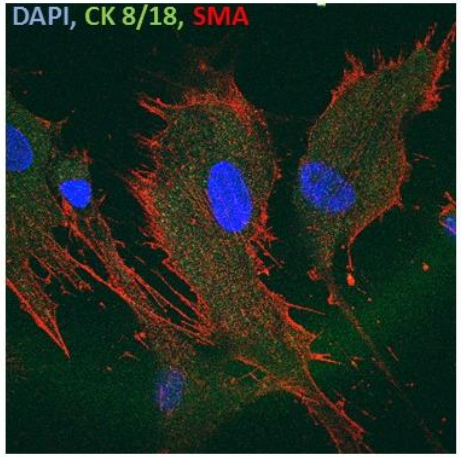
- **Developing Epithelial to mesenchymal transition model: plays major role in Cancer metastasis**
- We have engineered regulated model of human EMT currently being characterized for phenotypic screens thus allowing us to perform unbiased screens!

The EMT model generated will be useful for

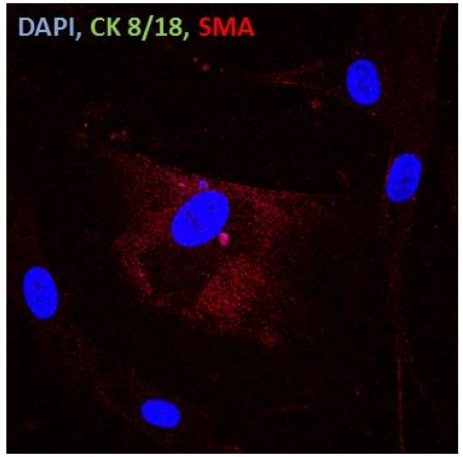
- target discovery or validation,
- ID & screening of new drugs/combinations
- ID novel EMT/Metastasis biomarkers



At P# 0, prior to EMT induction, cells show strong positive (+++) staining for epithelial & minimal staining (+) for mesenchymal markers



At P# 1, after EMT induction cells show (+++) positive staining for mesenchymal markers and minimal (+) staining for epithelial marker



At P# 2, after EMT induction cells show (+++) positive staining for mesenchymal markers and negative (-) staining for epithelial marker

Some early evidence on the Epithelial to mesenchymal transition in our patented system.

CK8/18 – Epithelial marker

SMA – mesenchymal marker

(Applied for provisional patent)

SAPIEN BIOSCIENCES

Advancing Science, Personalizing Medicine

Thank You

Rachna Goyal, PhD
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