MEDGENOME

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Internal Quarterly Newsletter

Send us your feedback at : editor@medgenome.com

Management Speaks

Sam Santhosh
Founder and Chairman,
MedGenome

Last month we reinforced our position as the leader in genetic diagnostics and research in India by the launch of two tremendously valuable tests – the ctDNA based liquid biopsy test for cancer and the carrier screening test for inherited diseases. Both tests were developed in house by our team, with support and guidance from some of the leading hospitals in India. On the research services front, our cancer immunotherapy solution, OncoPept™ has been gaining traction in the U.S and Dr.Amit Chaudhuri's article on page 11 gives you an overview of how genomics and NGS technologies are impacting immunotherapy.

Kudos to Reena and her team for bringing out the first edition of our internal newsletter. The objective of this newsletter is to keep us all informed about the various developments in our company. However it is rather easy to start a newsletter – the real job is to make sure it continues regularly. That requires support from all of you; provide your suggestions, feedback and encouragement to the editorial team and make sure we don't miss an issue!

Highlights

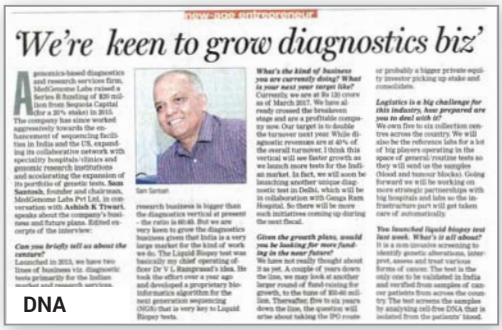
Most talked about

MedGenome launches 'ONCOTRACK', the Liquid Biopsy blood test for cancer recurrence detection and monitoring

MedGenome recently launched 'ONCOTRACK', the liquid biopsy based non-invasive screening test that is set to transform the way physicians in India can identify genetic alterations, interpret, assess and treat various forms of cancer. The test developed entirely by MedGenome, is the only one to be validated in India and verified from samples of cancer patients from across the country. The test screens the samples by analyzing cell-free DNA that is isolated from the patients' blood.

OncoTrack is a proven molecular tool after histopathology diagnosis and detecting molecular changes at baseline and at the time of relapse in lung and colon cancer for deciding the right treatment. The test has been validated in a scientific study, in academic collaboration with Tata Memorial Hospital- Dr Kumar Prabhash, Medical Oncologist and Dr. Amit Dutt, Principal Investigator (Scientist F) at ACTREC, Tata Memorial Centre.

From L to R : Dr. V.L. Ramprasad, COO, MedGenome; Mr. Sam Santhosh, Founder and Chairman, MedGenome; Dr. Kumar Prabhash, Associate Professor, Medical Oncology, TATA Memorial Hospital; Mr. Girish Mehta, CEO, MedGenome and Dr. Ramakant Krishnaji Deshpande, Vice Chairman, Asian Institute of Oncology, Mumbai


'We're keen to grow diagnostics biz'

DNA

http://www.dnaindia.com/money/interview-our-liquid-biopsy-is-only-one-to-be-validated-in-india-sam-santosh-2351804


the quint

#GoodNews: Bengaluru Lab's Biopsy Breakthrough To Help Cancer Care

GOOD NEWS

The Quint

https://www.thequint.com/medicine/2017/03/20/biopsy-cancer-medgenome-bengaluru-lab


New method to detect cancer when solid biopsy fails

By A Staff Reporter

Afternoon Despatch and Courier

MedGenome takes NIPT to tier 2 cities like Jaipur, Lucknow and Surat

MedGenome announced the launch of their latest solution MedGenome Claria in Jaipur, Lucknow, Surat and Coimbatore in February. MedGenome Claria is a unique and integrated solution of Non- Invasive Prenatal test (NIPT), which also offers free genetic counselling. The screening test analyses the cell free DNA of the fetus and gives out a detailed report for chromosomal abnormalities. The screening is non-invasive, extremely safe and is done by taking a small blood sample from the mother's arm. Due to the higher detection rate as compared to traditional screening tests, invasive confirmatory diagnostic procedures like amniocentesis and chorionic villus sampling are greatly reduced. To help ease the anxiety and clear the apprehensions of expectant parents, MedGenome Claria offers free consultation with expert geneticists to help expecting parents better understand the risks of genetic disorders and chromosomal abnormalities.

मेडजिनोम लाया हैं लखनऊ के लिये क्लेरिटी प्रसव पूर्व निदान के लिए एक क्रांतिकारी स्क्रीनिंग टेस्ट

लखनऊ। भारत के लिये यह समय नवीनतम और अच्छी प्रौद्योगिकी का उपयोग कर गुणसूत्र असामान्यता के बोझ और अभिव्यक्ति को कम करने का है। यह समय भारत में गर्भवता महिलाओं के लिये सबसे अच्छे तरीके से प्रसव पूर्व निदान के उनके मामलों के निपटान का है। मेडजिनोम, जीनोमिक्स संचालित अनुसंधान एवं निदान कम्पनी ने आज लखनऊ में अपने नवीनतम निदान मेडजिनोम क्लारिया के शुभारंभ की घोषणा की।

गर्भवती महिला को मदद करता है या पति-पत्नि को उनके बच्चे के आनुवांशिक स्वास्थ्य के बारे में गर्भावस्था के 9 वें सप्ताह में ही 99.9 प्रतिषत सटीकता से सम्पूर्ण मुक्त डीएनए का विश्लेषण करता है और किसी भी गुणसूत्र की असामान्यताओं के लिये एक विस्तृत रिपोर्ट प्रदान करता है। यह स्क्रीनिंग नॉन इनवेसिव, अधिक

Rahat Times

ANCHOR अजन्मे शिशु की सेहत को लेकर मेडिकल एक्सपर्ट्स ने कॉन्फ्रेंस में रखे विचार, कहा....

गर्भस्थ शिशु की सेहत जानने की एक्यूरेसी बढ़ी

...MEDICAL CONFERENCE

कॉन्फ्रेंस में क्रोमोजोमल डिसऑर्डर के कारण गर्भस्थ शिशु की सेहत पर शारीरिक और मानसिक रूप से पड़ने वाले प्रभावों के बारे में क्षृण मेडिसिन विशेषज्ञ डॉ. करुणा मंडल ने कहा कि गर्भस्थ शिशु की सेहत की सटीकता जानने की संभावनाएं बढ़ रही है। मेडिकल के क्षेत्र में इस तरह की जांचों

राजापार्क पत्रिका www.patrika.com

10 लाख बच्चे बीमारी के साथ जन्म लेते हैं

डॉ. वरुण ने बताया कि देश में हर साल 25 लाख से ज्यादा बच्चे जन्म लेते हैं। इनमें 10 लाख से अधिक बच्चे अनुवांशिक बीमारियों के साथ पैदा होते हैं, लेकिन जागरूकता की कमी, अज्ञानता, हिचकिचाएं और प्रसव पूर्व स्क्रीनिंग परीक्षणों की कम समझ के कारण लोग इस तरह की बीमारी से अनभिज्ञ रहते हैं। ऐसे में • अब माता-पिता डॉक्टर्स के मार्गदर्शन में प्रसव पूर्व स्क्रीन टेस्ट (एनआईपीटी) से गर्भस्थ शिशु की सेहत के बारे में जानकारी ले पता लगा सकते हैं।

होटल मेडजीनोम की ओरसे आयो उन्होंने कहा कि है कि उसके होने कैसी है? ऐसे मे शिशु की सेहत प्रसव पूर्व परिक्ष बनाया है।

इसमें गर्भा ही 99.9 प्रति वाले बच्चे के अ बारे में पता ल मेडजीनोम क्ली जांच के लिए ग से ब्लड सैंपल बैंगलुरु स्थित जाता है। वहां ब जरिए शिशु में बीमारी का पता लगाया जाता है।

है। मेडिकल के क्षेत्र में इस तरह की जांचों को बेहतर बनाने पर शोध किया हा है। यह बात क्रोमोजोमल गॉर्डर के कारण गर्भस्थ शिशु की सेहत पर शारीरिक और मानसिक रूप से पड़ने वाले प्रभावों के बारे में क्षृण मेडिसिन विशेषज्ञ डॉ. करुणा मंडल ने कही। हाल ही में राजापार्क स्थित एक

Rajasthan Patrika

ભાસ્કર વિશેષ બેંગલોરની આઘતન લેબોરેટરી પ્રિનેટલ નિદાન માટે એક ક્રાંતિકારી સ્ક્રીનિંગ ટેસ્ટ સુરતમાં લાવી

રંગસૂત્રમાં ખામી 9 સપ્તાહના ગર્ભમાં જાણી શકાશે

સ્ક્રીનિંગ ટેસ્ટમાં માતાના લોહીનો નમૂનો

બાળકના આરોગ્યની ખાતરી કરી શકાશે

Divya Bhaskar

MedGenome launches Claria carrier screening for the Indian population

MedGenome recently launched Claria Carrier Screening Test. The test,developed in-house by MedGenome, in association with Sir Ganga Ram Hospitals and under the guidance of Dr. I.C Verma,has been validated by clinicians, and will be available across India in over 500 hospitals.The test provides vital information of "Carrier" status to couples and their risks of passing down recessive diseases (condition where a person has two copies of an abnormal gene) to their child. Based on superior NGS (Next Generation Sequencing) Technology the Claria Carrier Screening test can detect over 1300 recessive diseases and disease-causing variations. In addition MedGenome Claria has a dedicated expert genetic counselling unit, which offers absolutely free genetic counselling to help couples understand key genetic information while planning for a baby.

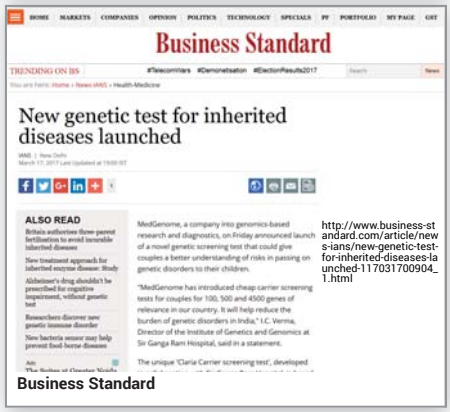
From L to R: Dr. Ramprasad, COO, MedGenome Labs Pvt. Ltd,
Mr. Sam Santhosh, Chairman, MedGenome Labs Pvt Ltd,
Dr. I.C. Verma, Director, Institute of Genetics, and Genomics, Sir Ganga Ram Hospital
Dr. Seema Thakur D.M. (Medical Genetics), HOD & Senior Consultant, Fortis Hospital


भारत के लोगों को विरासत में मिली जैनेटिक बीमारियों का मिला उपचार

हर साल भारत में 10 लाख बच्चे जेनेटिक बीमारियों से पीड़ित

उपस्थित गणमान्य।

Dainik Savera


Business Standard

New genetic test for inherited diseases launched

ALSO READ

http://www.business-standard.com/article/news-ians/new-genetic-test-for-inherited-diseases-launched-117031700904_1.html

Business Standard


ET Healthworld

MedGenome announces the launch of Claria Carrier Screening test

http://health.economictimes.indiatimes.com/news/industry/med-genome-announces-the-launch-of-claria-carrier-screening-test/57699335


New genetic test to detect inherited diseases launched

New Delhi: A new genetic test for inherited diseases has been launched by MedGenome, a company into genomics-based research and diagnostics, on Friday.

This new test could give couples a better understanding of risks in passing on genetic disorders to their children.

IC Verma, Director of the Institute of Genetics and Genomics at Sir Ganga Ram Hospital, said in a statement. "MedGenome has introduced cheap carrier screening tests for

ZEE NEWS

MedGenome in News

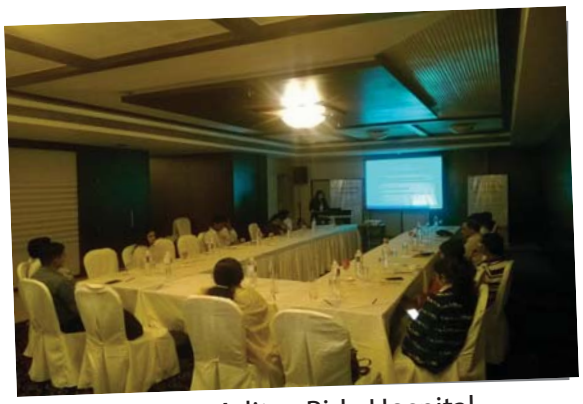
1. **MedGenome expansion story in Telangana Today**
   http://telanganatoday.news/medgenome-plans-pan-india-expansion
2. **MedGenome story in Yourstory**
   https://yourstory.com/2017/03/medgenome-startup/
3. **Authored article by Dr Ram on Genomics and Future of Medicine in Business Today**
   http://www.businesstoday.in/magazine/features/genomics-and-future-of-medicine/story/243003.html
4. **Mr Girish Mehta talks about NIPT in The Hindu Business Line**
   http://www.thehindubusinessline.com/specials/pulse/decoding-those-genes-and-your-babys-health/article9571008.ece
5. **Authored article by Dr Priya on Not a safe bet in The Hans India**
   http://www.thehansindia.com/posts/index/Sunday-Hans/2017-03-19/Not-a-safe-bet/287743
6. **Budget expectation for 2017 from Mr Surajit Chakrabartty in Business Standard**
   http://www.business-standard.com/article/b2b-connect/foster-ppp-to-percolate-benefits-of-affordable-healthcare-to-the-masses-117012000813_1.html

MedGenome Connect

MedGenome has been creating awareness on the relevance of genomics in clinical practice for the last few years. We have been engaging the medical fraternity, thought leaders, academic institutes, research centres,hospitals and policymakers at multiple levels to create awareness on how genomics based diagnostics can prove to be an effective tool in their routine clinical practice.

MedGenome currently works with more than 800 doctors and 500 hospitals across the country.Our team spans across all the regions and interacts with the doctors in tier-I and tier-II cities supported by our pan- India logistics network.

In Jan- March quarter we conducted more than 25 CME's which were attended by more than 400 clinicians across specialities ranging from oncology, gynaecology, gastroenterology, obstetrics, neurology and others. These CME's were conducted across India in more than 10 cities.



Pune - Aditya Birla Hospital

Kolkata - Fluyurs

Chennai - Apollo Speciality

Ahmedabad - Pride Plaza

Making a difference

When Nishka Hosangady started school at 3 years, she seemed perfectly normal. But, as she grew it was found that she had soft neurological issues. Her parents took her to every possible doctor suggested, but there was no visible improvement in her condition and she gradually withdrew from her social circle. Her parents consulted Dr. Charulata Sankhla, an adult movement disorder specialist, who suggested to get her tested using a new dystonia panel from a lab in Bangalore called MedGenome. They took Nishka's blood sample and after 3 months she was diagnosed with Benign Hereditary Chorea, which is a rare autosomal disorder.

To know the complete story please browse throug the link below:

http://www.patientsengage.com/personal-voices/we-struggled-10-years-find-out-whats-wrong-our-child

From our U.S office

Our U.S lab focuses mainly on cancer immunotherapy along with other genomic services. The past decade has shown immense focus on this emerging area and we have developed OncoPept™ and OncoMD – our key products that help to provide genomic insights into the tumor mutanome.

The year began with a series of events and conferences.

Starting with our participation at the Precision Medicine World Congress and Outsourcing in Clinical Trials (ARENA) conference, we presented our first poster at Frontiers in Cancer Immunotherapy organised by the prestigious New York Academy of Sciences (NYAS).

In the next quarter we plan to participate in 5 events - namely: The AACR Annual Meeting, Global Capital Summit, PEGS Summit 2017, Thirteenth Annual Biomarkers and Immuno-Oncology World Congress and 77th Scientific Session of the American Diabetes Association.

We are presenting our abstracts and posters in the following conferences:

• For AACR - A novel algorithm to identify TCR-binding somatic mutations from human cancers
• For PEGS Summit and the Thirteenth Annual Biomarkers and Immuno-Oncology World Congress - A multi-compartmental genomics approach to discover tumor cell vulnerabilities for immune-mediated elimination
• For American Diabetes Association- Diabetome: A Novel Clinical Database and Analytic Platform Based on 300,000 Individuals with Diabetes

We also hosted 2 symposiums - one each in February and March, where distinguished doctors spoke. Dr. Sandosh Padmanabhan of University of Glasgow and Dr. Matthew Wheelerof Stanford University, spoke about cardiac genomics in the first ever symposium held at our U.S lab. This was followed by talks on cancer genomics from Dr. Pramod Srivastava ofUniversity of Connecticut Health and Dr. Beatrix Ueberheide of NYU School of Medicine.

Sam Santosh was invited to speak at Startup Tea Talk (a series of monthly event hosting, in association with SF Founder's Club SVTeahouse, and the blog for Silicon Valley Startup Story together with DingDing TV, and couple other partnering organizations). Sam spoke about the MedGenome journey and his plans for MedGenome's future in genomics.

Rational use of biomarkers in oncology clinical trials: A paradigm shift towards precision medicine

Amit Chaudhuri, VP R&D, MedGenome Inc. USA

Background

Biomarkers are biological indicators of early disease detection (diagnostic), disease progression and outcome (prognostic), and response to therapy (predictive).

The inclusion of biomarkers in patient selection has led to superior drug response rates and increased overall survival in pivotal clinical trials. Also, use of biomarkers to select drug sensitive patients have greatly improved the quality of life by improving therapeutic efficacy and reducing toxicity. Biomarkers discovered and used in clinical trials have been approved as companion diagnostics and used routinely in making treatment decisions.

In this review, I will give an overview of cancer biomarkers, their discovery using traditional approaches and more recently through genomics and proteomics technologies and their validation through clinical trials.

Definition of biomarkers

Diagnostic biomarkers

Diagnostic biomarkers allow disease detection and/or disease staging. Traditionally, diagnostic biomarkers in cancer came from histopathology. The WHO classification of solid and hematological tumors are based on histopathological examination of the tissues and available as monographs, or blue books for consultation (whobluebooks.iarc.fr/). For example, WHO recognizes 30 subtypes of lymphoma based on their histopathology, which has improved the accuracy of patient diagnosis significantly, without impacting drug development, or treatment decisions, because of molecular heterogeneity within the subtypes [1].

For example, gene expression profiling of diffuse large B-cell lymphoma (DLBCL) has identified three distinct molecular subtypes that are treated differently. Other molecular rearrangements have aided in the diagnosis of solid tumors such as ALK-fusion for the diagnosis and therapy of ALK-positive non-small cell lung cancer. Diagnostic markers in many instances have become both predictive and prognostic. For example, estrogen receptor positive (ER+) breast cancer is a diagnostic marker, as well as a predictive marker for hormone inhibition therapy, and a prognostic marker of good clinical outcome, when compared with hormone receptor negative tumors [2].

Predictive vs. prognostic biomarkers

There is considerable confusion in our understanding of what distinguishes a predictive biomarker from a prognostic biomarker. Predictive biomarkers are associated with response to treatment. Tumors positive for the marker will show differential treatment effects compared with tumors negative for the marker. As an example, in non-small cell lung cancer (NSCLC), tumors harboring activating mutations in epidermal growth factor receptor (EGFR) benefited more from erlotinib (Tarceva) treatment (hazard ratio, HR 0.10) compared to tumors harboring wild-type EGFR treated with erlotinib (HR 0.78)[3]. In this example, both groups benefited from treatment HR <1, however, there was a quantitative difference in benefit between EGFR mutant vs. EGFR wild-type group (quantitative interaction) [2, 4]. The benefit can also be qualitative, in which case the biomarker positive group benefits from the therapy, whereas there is a lack of benefit to the negative biomarker group including harmful effects from the treatment.

For example, use of anti-EGFR monoclonal antibody cetuximab provides benefit to metastatic colorectal cancer patients harboring wild-type KRAS, but patients harboring mutant KRAS fare poorly in the presence of the drug [5]. This makes KRAS a predictive marker of response to anti-EGFR therapy in metastatic colon cancer. Surprisingly, the status of KRAS is not a predictive biomarker of anti-EGFR tyrosine kinase inhibitor (erlotinib or gefitinib) in non-small cell lung cancer [6] indicating deeper biological differences between the two cancer types.

A prognostic biomarker provides information on disease outcome, such as disease progression, disease recurrence or death, independent of drug treatment [2]. For example, activating mutations in phosphatidyl-inositol-3-kinase catalytic subunit alpha (PIK3CA) show worse prognosis in women with HER2-positive metastatic breast cancer, regardless of treatment [7, 8]. A prognostic biomarker may reveal the underlying mechanism of disease progression and can guide the development of novel therapies.

Biomarker detection in clinical settings

Platform technologies

Biomarkers are derived from tumor tissues or other body fluids and detected by histopathological, immunohistochemical (IHC), fluorescence, ELISA, and PCR based techniques. Tumor tissue-derived biomarkers, such as overexpression of genes are detected by IHC, such HER2 overexpression in HER2+ breast cancer. Chromosomal translocation such as BCR-Abl fusion in Philadelphia chromosome is detected by fluorescence in situ hybridization (FISH). ELISA methods are used to detect proteins in blood or other body fluids such as Carbohydrate antigen 19-9 (CA19-9) from the serum of pancreatic cancer patients. More recently DNA and RNA sequencing have expanded the scope of biomarker detection from limited tissue material. Mutations in EGFR, BRAF, KRAS and other oncogenes are detected by sequencing and is used routinely in clinical settings as predictive and prognostic markers. Similarly, mass-spectrometric approaches have identified biomarkers in complex body fluids such as serum and saliva. Biomarkers discovered using high throughput proteomics methods are validated in the clinic using more robust multiplex ELISA methods.

Multi-omics approaches

In recent years, technological breakthroughs in genomics and proteomics have resulted in a shift from the use of a single biomarker to multiple biomarkers for disease classification, diagnostics, and prognosis. This is specifically true for oncology indications, where genetic and biochemical heterogeneity of tumor cells and the need to use combination therapies to derive maximum efficacy require a deeper understanding of the molecular features of the tumor and its microenvironment. These molecular features can be accurately assessed by the use of carefully selected biomarkers.

This multi-omics biomarker discovery approach has found extensive application in the area of cancer immunotherapy – a rapidly developing field of cancer treatment, where the host immune response is boosted to elicit an anti-tumor response. The efficacy of immune-boosting checkpoint inhibitors is closely associated with molecular features present in tumor cells and the tumor microenvironment. Both exome and RNA-sequencing analyses reveal critical determinants of drug response. The scope of such an analysis is schematically represented in Figure1.

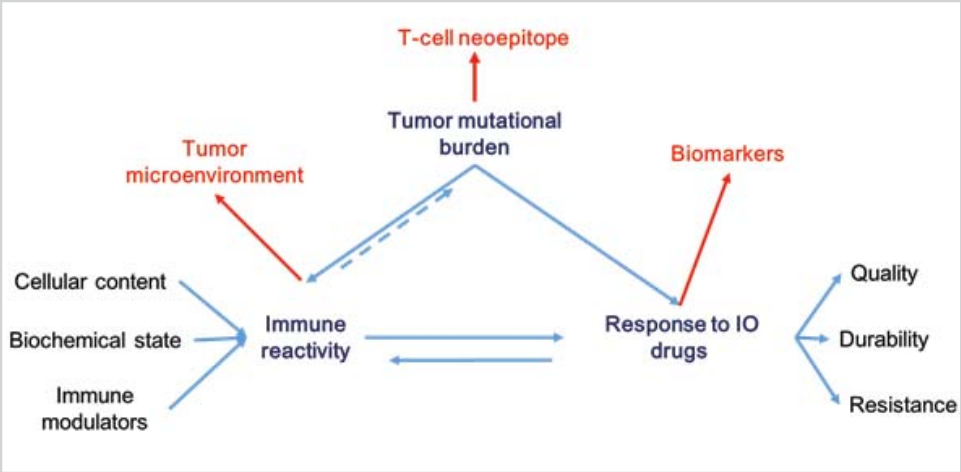


Figure 1. Biomarkers of response to immuno-oncology drugs combine analysis of tumor cell intrinsic and extrinsic factors. Exome sequencing identifies protein-altering genetic changes in tumor cells that contribute to the generation of immunogenic peptides (T-cell neoepitopes) mediating recognition between tumor cells and cytolytic killer T-cells (CD8 T-cells). Whole transcriptome sequencing provides information on the tumor microenvironment defining the immune reactivity of the tumor. Together, the tumor cell and tumor microenvironment analysis determines response to cancer immunotherapy drugs [9-11]

Biomarkers make meaningful differences in clinical trials

A review of clinical trials conducted between 2006-2015 (9985 trials) reveal a low Phase-I to approval success rate for oncology drugs compared to other non-oncology disease areas (5.1% vs. 11.8% respectively) [12]. Further, the success of a biomarker-driven clinical trial was 3-times higher than a trial without biomarkers (25.9% vs. 8.4% respectively) [12]. Therefore, biomarker discovery has become mandatory for the clinical development of therapeutic molecules in all disease areas, particularly in oncology.

Biomarkers have become particularly important for targeted therapies and patient selection during clinical trials. In the early days of cancer treatment, non-targeted therapies, such as chemotherapy, or radiation therapy did not require specific biomarkers for patient selection. Histopathological examination of tumor tissue helped in tumor staging, which guided treatment decisions. With the advent of targeted therapies, biomarkers for selecting patients who will benefit from treatment became pivotal in designing Phase-II and III clinical trials. In 2005, AstraZeneca's EGFR inhibitor gefitinib was tested in a Phase-III multicenter clinical trial involving 1692 patients. The trial failed to show improvement in benefit between the placebo and the treated groups, although indications of benefit to certain patient subgroups, such as never smokers or Asian origin were noted [13]. However, follow up molecular studies, investigating the mechanism for the lack of benefit, discovered that only patients harboring activating mutations in EGFR were super responsive to the EGFR tyrosine kinase inhibitors erlotinib and gefitinib [14-16]. These findings resulted in the rescue of the drugs, which have become the standard of care treatment for NSCLC patients harboring activating mutations in EGFR. Similarly, approval of crizotinib against NSCLC tumors harboring anaplastic lymphoma kinase fusion (ALK-fusion) has become the standard of care treatment within four years after the discovery that 3-5% of NSCLC tumors harbor ALK-fusion genes [17] and ROS fusion genes [18]. Such accelerated clinical development was only possible because biomarkers for selecting tumors that will benefit from therapy were well established and FISH assays to detect such fusions were in place.

Biomarkers for drug repurposing

Drug repurposing or drug repositioning is finding new uses for existing drugs against new disease indications. Repurposed drugs may be approved for one disease indication, or may have failed clinical development due to inadequate efficacy or unacceptable toxicity. An example of an approved drug repurposed for a totally different indication is the cyclogenase-2 inhibitor (COX2) Celebrex (celecoxib). Celebrex and its generic counterpart celecoxib reduce inflammation and is approved for osteoarthritis, rheumatoid arthritis and acute pain and other indications. However, the drug has been repurposed for use against colon polyps based on the finding that COX2 overexpression increases the risk of colorectal cancer and a clinical trial to that effect demonstrated a decrease in the risk of additional polyp formation in individuals with colorectal cancer [19]. Drug repurposing requires identification of diagnostic biomarkers associated with disease mechanisms. In the example above, the discovery that COX2 is highly overexpressed in colon cancer and inflammation is a key mediator of colon polyp formation led to the repurposing of COX2 inhibitor in this disease indication, which is considered a milestone discovery in colon cancer research. Another example is the use of the Type-2 diabetic drug metformin in preventing cancer. Metformin inhibits mitochondrial complex-I, reducing the generation of ATP, thereby increasing AMP levels that trigger AMPK kinase activation resulting in an increase in glucose metabolism [20].

New discoveries made in the last few years have identified pleiotropic effects of metformin on cellular pathways, such as inhibition of reactive oxygen species (ROS) generation, inhibition of p53-mediated cyclin-D1 expression, inhibition of autophagy and insulin-like growth factor signaling triggering a flurry of over 200 clinical trials in cancer (www.clinicaltrials.gov). Drug repurposing will rely heavily on the discovery of biomarkers for patient stratification, and for measuring positive effect of drugs in the repurposed disease indications.

Future of biomarkers in precision medicine and personalized therapies

Biomarker discovery is a critical bottleneck to ensure the success of drugs in clinical trials. The cost of new drug development has skyrocketed in the last decade reaching over 1 billion dollars in discovery/development cost and running clinical trials. The burden of failure in late stage clinical trials results in a significant erosion in company's market value, winding down of future research activities and blunting innovation that small companies bring to the table. A recent example is the failure of BMS's drug Opdivo (nivolumab) in the first line treatment of advanced non-small cell lung cancer. The results of the failed clinical trial demonstrated that PD-L1, which is used routinely as a biomarker for selecting patients might not be robust enough to ensure approval of BMS's drug. The lack of positive clinical trial data erased 20% of BMS's market cap in a day and prevented the market adoption of its drug to a competing product Keytruda (pembrolizumab) from Merck, which got approved for the same indication.

The Opdivo CheckMate trial and other unsuccessful clinical trials emphasize the need to identify robust biomarkers very early during drug development, and design efficacy and toxicity studies around these biomarkers to evaluate their utility, before transitioning the drug into pivotal clinical trials.

A large number of technological platforms including next generation sequencing and mass-spectrometry are available for the rapid discovery of biomarkers in complex tissues and body fluids [21]. This robustness of these technologies is well suited for clinical adoption and is rapidly gaining momentum with the regulatory authorities. Equipped with multi-omics-based biomarkers the era of precision medicine will enter into the next phase of delivering personalized medicine, where each patient will receive a tailored therapy at the right time and at the right dose to maximize efficacy and avoid adverse toxicity – fighting cancer and still experiencing a better quality of life.

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Carrier screening

By Dr. Sandhya Nair, Senior Genome Analyst

Screening genetic disorders in India has gained prominence in recent years. With the greater awareness about genetic disorders among young couples in India, there is an increasing demand for carrier screening. Carrier screening plays an important role when it is performed either preconception or during pregnancy to know a couple's risk of having a child with a recessive genetic disorder.

Implementation of carrier screening program among the Ashkenazi Jewish population helped in avoiding marriages between carriers of Tay-Sach disease, reducing the incidence of the disorder significantly.

Considering large population of India, high birth rate and inbreeding in few communities the prevalence of genetic disorders is relatively high. The most commonly inherited genetic disorders in India include hemoglobinopathies, congenital adrenal hyperplasia, glucose-6-phosphate dehydrogenase deficiency, neuromuscular disorders, inborn errors of metabolism, cystic fibrosis etc. Hemoglobin disorders are considered to be a serious health problem by WHO. The carrier frequency of beta thalassemia is reported to vary between 1-17% (mean 3.3%). It is estimated that about 10,000 babies affected with beta thalassemia are born every year (Kapoor et al, 2010). Leading organisations such as ACMG and ACOG recommend screening for disorder mainly based on demography, extent of inbreeding in the population, ethnicity and prevalence estimates of recessive diseases in the population.

Most laboratories offer screening of a particular mutation or a set of mutations and not the entire gene due to associated cost. These targeted assays provide limited information due to sequencing of few target regions. Next generation sequencing provides screening larger number of genes at a time, with faster turn around time and greater chances of incidental findings making it more cost effective. On the 17th of March, MedGenome launched Claria carrier screening test which offers systematic carrier screening using next generation sequencing and custom designed gene panel that includes genes which are known to cause common as well as rare diseases.

Carrier screening is of great importance as it helps in early diagnosis, timely intervention (prevention, management, treatment), determines the risk of conceiving a child with inherited disorder, prevents death, markedly reduces disease severity, improves quality of life, substantially benefits psychosocially and most importantly gives an opportunity to make informed decision.

From our Colleagues

Understanding Financial Management

By Hemant Jain, Deputy Manager - Finance & Accounts

Do you think finance is beyond our realm! Is it all about compiling data and preparing statements? If so, you are confusing accounting with finance. The ability to take financially intelligent decisions is what financial management is all about.

We are constantly making financial decisions whether we realize it or not. All of us work towards a common goal - profitability. The goal can be achieved only if we understand the impact of each one of our actions on the organization's bottom line & ensure that we take all those necessary steps to only strengthen the bottom line and not vice - versa.

In my opinion, it is those actions that generate profit that constitute financial management and not those that calculate profit.

Irrespective of whether you are the owner or a mere employee, you have the power to affect the bottom line. So when anyone says, 'I am a non-Finance Person', it is equivalent to saying 'I don't care what the financial outcome of my actions is going to be'. But that's very strange. You must never do anything without understanding how it will affect the organizations profitability!

So what exactly is Good Financial Management? The answer to this question can be very long and include every principle of financial management. Let me give you, instead, a short and succinct formula in the form of two rules for what, in my opinion, comprises good financial management.

Let's call them two golden rules of good financial management.

The first rule: Never invest your money without ensuring that the assets you acquire can generate a return which is at least equal to the cost of your capital.

"Two golden rules of good financial management."

What you must remember is that of all the sources, none are free. The money that an organization raises comes at a cost. Very often we lose sight of this cost, and then pay a price that is far too high. Don't forget, there are no free lunches in this world!

The first golden rule urges you to invest only after ensuring that the returns you can generate are either equal to, or preferably greater than, the corresponding cost of sources.

The first rule:

> ***Never invest your money without ensuring that the assets you acquire can generate a return which is at least equal to the cost of your capital***

The second rule:

> ***Invest your money in such a way that the assets will generate an inflow of funds before the liabilities demand an outflow. Remember, Profit & money (cash) are two different things.***

You must recognize that in a business, all sources of funds are liabilities and not gifts. The money you have raised today will have to be repaid tomorrow.

These two rules implies knowledge on your part about your cost of capital and an ability to project the returns that can be generated through the deployment of your funds. Similarly being constantly aware of the need to be able to return the money when it becomes due will make you alert to putting it to the best possible use in the time given to you to use it.

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