Metachip: next-generation liquid biopsy for 18 types of cancer

ConquerX develops a minimally invasive blood test that can detect up to 18 types of cancer based on cutting-edge microRNA sensor technology.

Problem

Cancer kill 8 million people around the world every year and 14 million more will develop the disease. In the US, one in five people will die of some type of cancer. One-third of these deaths can be averted by routine screening and early detection of the cancer when it is most treatable. Unfortunately, with a few exceptions, there is no accurate, minimally-invasive, cost-effective and portable method to early detect the majority of cancers, including the more lethal types such as brain, ovarian or pancreatic cancer.

Technology

a. Metachip

The MetaChip is an optimized electrochemical biosensor that use blood sample to detect microRNAs linked to eighteen types of cancer: lung, pancreas, breast, kidney, bladder, liver, prostate, esophageal, gastric, colorectal, cervical, glioblastoma, ovarian, thyroid, hepatocellular, oral, Kaposi's sarcoma and non-Hodgkin lymphoma. The Metachip workflow has three simple steps: draw blood, place the blood on the Metachip, and put the Metachip on a portable sensor-reader to get results in 15 minutes.

b. MicroRNAs

MicroRNAs (miRNAs) are small, noncoding RNA sequences of about 18-22 nucleotides[1,2] . They influence numerous cancer-related processes such as proliferation, cell cycle control, apoptosis, differentiation, migration and metabolismo[3-6,8]. In addition, miRNA expression fingerprints correlate with clinical and biological characteristics of tumours, including tissue type, differentiation, aggression and response to therapy [10,11] .

These characteristics, coupled with the stability of miRNAs in blood, serum, saliva, tears and other types of body fluids, make them an excellent candidate to serve as cancer biomarkers[7-9]. However, because of the small amount of circulating miRNAs and the large amount of proteins in blood, miRNA extraction and quantification is technically challenging[16]. Several techniques such as northern blotting, molecular cloning, microarrays, and quantitative polymerase-chain reaction (qPCR), as well as next-generation sequencing, are used to detect microRNAs[12,13]. However, these methods have either low throughput, low sensitivity, are costly, require a large amount of total RNA or/and often involve laborious sample handling protocols that cannot be performed without highly trained personnel[12,14,15]. Such limitations severely hinder the application of existing miRNA detection methods into clinical practice. With prorietary electrochemical biosensor technology, the Metachip can overcome these limitations.

Preclinical Studies

Our published preliminary research demonstrates that the Metachip's early prototypes are capable of identifying tiny nucleic acid fragments such as DNA nucleotide sequences at very low concentration level with high sensitivity. The first prototype is an ultrasensitive electrochemical DNA biosensor to detect human papillomavirus (HPV) type-34 and -73[22,23]. When tested on biological samples, the chip showed a detection limit of 5.967×10^{-17} M of target DNA, which is lower than that of existing instruments.

We then conducted a small pilot to test the detection of microRNA-155, a biomarker highly expressed in earlier stages of breast cancer. The test was able to detect breast cancer with a sensitivity of 83%, specificity of 100%, and accuracy of 90%. Our next step is to conduct a larger pilot study on lung cancer blood samples ($n \geq 100$) to define Metachip's optimization curves for concentrations and recognition of microRNAs, analytical sensitivity, analytical specificity, detection system limit, clinical sensitivity and clinical specificity.

Industry & Competition

We anticipate companies such as Autolab, Metrohm and Edaq as chain partners to the hardware development, as well as companies in the lab testing and insurance sectors such Quest Laboratories and/or Labcorp, and Center for Medicare & Medicaid Services (CMS) as chain partners to our business model. On the other hand, we have competitors who are in the R&D phase of developing liquid biopsy tests using a variety of methodologies and biomarkers. However, they face challenges, especially in pricing, because of time and money-consuming requirement of laborous sample preparation process for RNA/microRNA extraction by trained personnel.

Our patent-pending scientific assets are the key drivers for the business, giving us a competitive advantage jointly with our price point of $350 or less, which can be 3 times less than our main competitors. The Metachip is the first and only test of its kind to detect eighteen different types of cancer in a single blood-based test. It is also the first to detect miRNAs with electrochemical biosensor designed specifically for clinical applications. The Metachip has a combination of nanostructures and polymers that allows it to detect, with high sensitivity and specificity level, sequences of nucleic acids in very low concentrations without any need for sequencing and PCR. The workflow of the test does not involve sample preparation or need for trained personnel. The result can be delivered not in the same day of testing, but in the same hour.

Team

Our ConquerX team met at MIT Sloan School of Management in 2015 during a Global Entrepreneurship program. We are a diverse team who have a combination of more than thirty years of experience in biomedical sciences, engineering & business. Our

CEO, Luis Trapani, is a serial entrepreneur and experienced private equity manager who have a track record of successfully launched and led new projects. Deborah Zanforlin, the inventor of the technology, is a biology professor from Brazil and have 5 years of experience in bio-sensor engineering to detect diseases. She is overseeing the building of the prototypes and R&D with Jakub Chudik, the third cofounder who is an engineering student at MIT and have experience in robotics and engineering.

The fourth co-founder, Jorge Sanchez, is also a serial entrepreneur with more than ten years of B2B sales and channel development experience. He will oversee channel development with customer labs and hiring of sales team. Last but not least, To-Nhu Huynh has a Master in Healthcare management and policy from the University of Texas and is currently working in cancer control programming at MD Anderson Cancer Center. She manages the R&D strategic partnerships and research protocols.
Our advisor, Issac Stoner, is the Healthcare Practice Leader at the MIT Martin Trust who had co-founded & led a company specializing in microRNA assays to successful exit.

Regulatory Landscape

Our main regulatory partners are the FDA and the CMS. We already met and discussed the FDA application with the FDA Branch Chief of Molecular Diagnostics to review the regulatory pathway for the Metachip. Strategically we will start the FDA approval process with FDA-cleared as IVD testing 510(k), anticipating with or without premarket approval application (PMA). We will also work with CMS, the largest insurer in the U.S., to get approval for reimbursement of the test on the same category as other preventive services such as a screening mammogram.

Market Opportunity & Business Model

We position the Metachip as a routine screening test to prevent later-stage cancer in healthy individuals who are at risks cancer. In the U.S., the number of such individuals is estimated to be around 64 million. At a starting price of $350 per test, the total addressable market in the U.S. is up to $22 billion. Combined with the Asian and European cancer screening market, the market is over $100 billion.

We will sell the metachip readers and consumables to the labs, and the labs pay for each test they perform. Each test will be priced at around $350. We reach our customers through indirect channel approach by reaching partnership agreement with CLIA-certified lab, with a dedicated sales team to approach physicians as influencers with veto power and engage with the general public, cancer patients and families. In the healthcare sector, R&D is our main cost stream. Our main revenue comes from selling test panels, first in the USA and then international expansion, targeting a gross margin of 85%, with a gross profit of $210 per unit sold.

References

[1] Lee RC, Feinbaum RL, Ambros V. The C. elegans heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14. Cell [Internet]. 1993;75:843–54. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8252621

[2] Filipowicz W, Bhattacharyya SN, Sonenberg N. Mechanisms of post-transcriptional regulation by microRNAs: are the answers in sight? Nat Rev Genet. 2008;9(February):102–14.

[3]Ha M, Kim VN. Regulation of microRNA biogenesis. Nat Rev Mol Cell Biol [Internet]. 2014;15(July):509–24. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25027649

[4] Xiao C, Rajewsky K. MicroRNA control in the immune system: basic principles. Cell [Internet]. 2009 Jan 9 [cited 2012 Oct 27];136(1):26–36. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19135886

[5] Nelson PT, Wang WX, Rajeev BW. MicroRNAs (miRNAs) in neurodegenerative diseases. Brain Pathol. 2008;18:130–8.

[6]Hébert SS, De Strooper B. Alterations of the microRNA network cause neurodegenerative disease. Trends Neurosci. 2009;32(March):199–206.

[7]Shen J, Stass S a, Jiang F. MicroRNAs as potential biomarkers in human solid tumors. Cancer Lett [Internet]. Elsevier Ireland Ltd; 2012 Nov 26 [cited 2012 Dec 4];(December). Available from: http://www.ncbi.nlm.nih.gov/pubmed/23196059

[8]Jansson MD, Lund AH. MicroRNA and cancer. Mol Oncol [Internet]. Elsevier B.V; 2012 Oct 9 [cited 2012 Nov 13];6(6):590–610. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23102669

[9]Cissell K a, Deo SK. Trends in microRNA detection. Anal Bioanal Chem [Internet]. 2009 Jun [cited 2012 Nov 1];394(4):1109–16. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19367400

[10]Calin G a, Croce CM. MicroRNA signatures in human cancers. Nat Rev Cancer. 2006;6(November):857–66.

[11]Chen B, Li H, Zeng X, Yang P, Liu X, Zhao X, et al. Roles of microRNA on cancer cell metabolism. J Transl Med [Internet]. Journal of Translational Medicine; 2012 Jan [cited 2014 Feb 23];10(1):228. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3563491&tool=pmcentrez&rendertype=abstract

[12]Ren Y, Deng H, Shen W, Gao Z. A highly sensitive and selective electrochemical biosensor for direct detection of microRNAs in serum. Anal Chem. 2013;85:4784–9.

[13]Lee LIKWEE, Zhang S, Etheridge A, Ma LI, Martin D a N, Galas D, et al. Complexity of the microRNA repertoire revealed by next-generation sequencing. 2010;2170–80.

[14]Yin H, Zhou Y, Zhang H, Meng X, Ai S. Electrochemical determination of microRNA-21 based on graphene, LNA integrated molecular beacon, AuNPs and biotin multifunctional bio bar codes and enzymatic assay system. Biosens Bioelectron [Internet]. Elsevier B.V.; 2012;33(1):247–53. Available from: http://dx.doi.org/10.1016/j.bios.2012.01.014

[15]Wang Z, Zhang J, Guo Y, Wu X, Yang W, Xu L, et al. A novel electrically magnetic-controllable electrochemical biosensor for the ultra sensitive and specific detection of attomolar level oral cancer-related microRNA. Biosens Bioelectron [Internet]. Elsevier; 2013;45:108–13. Available from: http://dx.doi.org/10.1016/j.bios.2013.02.007

[16]Brase JC, Wuttig D, Kuner R, Sültmann H. Serum microRNAs as non-invasive biomarkers for cancer. Mol Cancer [Internet]. BioMed Central Ltd; 2010;9(1):306. Available from: http://molecular-cancer.biomedcentral.com/articles/10.1186/1476-4598-9-306

[17]Lautnera G, Gyurcsányi RE. Electrochemical detection of miRNAs. Electroanalysys. 2013;0–20.

[18]Wang J. Electrochemical nucleic acid biosensors. Anal Chim Acta [Internet]. 2002 Sep 26;469(1):63–71. Available from: http://linkinghub.elsevier.com/retrieve/pii/S000326700101399X

[19]Wang Q, Zhang B, Lin X, Weng W. Sensors and actuators B: chemical hybridization biosensor based on the covalent immobilization of probe DNA on chitosan – mutiwalled carbon nanotubes nanocomposite by using glutaraldehyde as an arm linker. Sensors Actuators B Chem [Internet]. Elsevier B.V.; 2011;156(2):599–605. Available from: http://dx.doi.org/10.1016/j.snb.2011.02.004

[20]Ronkainen NJ, Halsall HB, Heineman WR. Electrochemical biosensors. Chem Soc Rev [Internet]. 2010 May [cited 2011 Oct 25];39(5):1747–63. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20419217

[21]Su L, Jia W, Hou C, Lei Y. Microbial biosensors: a review. Biosens Bioelectron [Internet]. Elsevier B.V.; 2011 Jan 15 [cited 2011 Jun 13];26(5):1788–99. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20951023
[22]Campos-Ferreira DS, Nascimento GA, Souza EVM, Souto-Maior MA, Arruda MS, Zanforlin DML, Ekert MHF, Bruneska D, Lima-Filho JL. Electrochemical DNA biosensor for human papillomavirus 16 detection in real samples. Analytica Chimica Acta. 2013 Dec 4; 804: 258-263.
[23]Campos-Ferreira DS, Souza EVM, Nascimento GA, Zanforlin DML, Arruda MS, Beltrao MFS, Melo AL, Bruneska D, Lima-Filho JL. Electrochemical DNA biosensor for the detection of human papillomavirus E6 gene inserted in recombinant plasmid. Arabian Journal of Chemistry. 2014 Jun 11. Available from: doi:10.1016/j.arabjc.2014.05.023