Glass-Laser Multiplexed Biosensor

2nd Newsletter

May 2017

glam-project.eu

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1. Introduction

GLAM project develops a device to monitor and diagnose genitourinary cancers in a personalized way, rapidly, and at low cost. Additionally, it is done in a less invasive and unpleasant way.

Currently, differential cancer diagnosis takes place daily in clinical settings for both patient stratification and monitoring patient responses to existing treatments. However, the outcome of this diagnosis is still poor, with many deficiencies and false positives and negatives due to the low sensitivity and specificity of available methodologies. Moreover, as new targeted therapies are available to patients and to oncologists, there is a need to improve personalized diagnosis and therapy (i.e. personalized medicine). Thus, personalized medicine increases the need and the urgency to have diagnosis, prognosis, and monitoring data in an ultra-sensitivity and fast enough way to allow oncologists to take the appropriate decisions before the disease and the patients get worse.

Accordingly, the main aim of the GLAM project is to develop a new diagnostic tool to detect biomarkers from biofluids, obtained in a non-invasive manner, specifically in urine and focusing on genitourinary cancers, enabling oncologists to take better treatment decisions. To this end, GLAM will develop an integrated device based on novel label-free photonic biosensors with ultra-sensitivity, simplicity of use, portability, multiplexing and low cost by simply applying a drop of urine and reading 10 biomarker levels.

There is a significant advancement in the technology behind the GLAM biosensor as well as its associated tasks and activities, including the next key aspects: photonics methodology, generation of new optic materials, biomarker and antibody generation, microring functionalization with antibodies, concept design of the integrated detector device, e-reader platform design, patient selection and collection of clinical samples, intellectual property rights management and patent application, dissemination of activities and first outcomes, and regulatory activities.

It is remarkable that GLAM partners have already reached a **preliminary proof of principle of the whole concept.**	Using a biosensor's prototype, **the first biomarker measurements** have been accomplished using the global GLAM methodology.	It is also notable that IPR data has been generated and used to define a **patent application based on the global technology of the GLAM project**.	This will warrant the **future commercialization of the GLAM Biosensor** and its use by oncologists worldwide in order to help them to take important decisions in personalized diagnosis and therapy monitoring of patients.

Importantly, the GLAM unique technology will make the device also usable with other biofluids aside of urine (serum, plasma, tears, saliva, synovial, peritoneal, and cerebrospinal fluid) and might also be used to help physicians in personalized medicine in many other biomarkers driven diseases, aside of cancer.

2. Main results

GLAM consortium already designed and generated the first prototypes of microring structures, biomarkers and antibodies in order to develop the novel photonic biosensors based on microring lasers. Moreover, antibodies have already been functionalized to the new microring structures. Additionally, contacts with oncologists have already started and this allowed to recruit the first patients for the clinical study and to collect some urine samples that will be used later for clinical validation of the biosensor.

The consortium already achieved the preliminary preclinical proof of principle with a soluble biomarker and its corresponding detecting antibody. This represents a very important step in the path to set up the tuned multiplexed platform to allow the detection of up to 10 different biomarkers without labelling, washing, or amplification steps, that will enable and guide clinical personalized treatment decisions from just a single small biological sample.

In order to integrate all the components in a small, easy-to-use, robust, fast, cheap, and single-step diagnostic device to be used in point-of-care settings, various activities have already lead to the design and generation of the first integrated chip prototype.

Finally, several aspects related to technical documentations are already implemented by all the consortium partners. They are using these new guidelines to generate additional GLAM device related information to be fully aligned and towards conformity with the essential requirement of the applicable EC Directives, which will serve as the regulatory basis for the CE Certification and ISO 13485 Certification of the finished In-Vitro Diagnostics GLAM Biosensor medical device.

3. By Work Package

Work Package 1: Biomarkers, biological tools (mAbs) and biological samples

The selection of biomarkers has been made, which led to the correct start of next tasks. The 10 most promising biomarkers were listed, ranked, and selected to start the generation of the recombinant biomarkers and use them to generate monoclonal antibodies for its detection. The scientists already have several antibodies that are validated and will be used in later phases of the project to set up the biosensor device. The rest of the antibodies will be generated during the upcoming months as stated in the working document.

Work Package 2: Optical biosensors: microring design and chemical functionalization

An analytical theoretical framework was developed and numerical tools were used to provide guidelines for the design of the microrings and waveguide. The optical performance of the microrings was tested by spectral transmittance spectroscopy. Several functionalization protocols have been tested to efficiently and selectively immobilize antibodies at the surface of the microrings. A “passive” sensing experiment was realized using the microrings.

Work Package 3: Fabrication of multiplexed microring resonator arrays & Chip packaging

In the GLAM sensor cartridge, ten channels will be implemented, each of them sensing a different cancer biomarker. A drop of urine will be introduced in the cartridge. Microfluidic channels will distribute it to the different sensing rings, immobilized with the different biomarkers antibody capturing layers. A beatnote will be generated in each channel and detected by relatively inexpensive readout electronics. Great efforts have been carried out to define the assembly procedure of the cartridge, since this procedure will impose some constraints to the chip design.

Work Package 4: Photon detection and integration: capture software & reader integration

Given that the value and shape of the beat note frequency is not known at the time of writing, a development demonstrator has been setup based on the expected value of 3 GHz, numerically anticipated by other partners. This setup will cover an even worst case scenario, being able to detect frequencies of up to 6GHz. It consists of a processing platform, an acquisition module and means of graphically presenting the value of the beat frequency in real-time, as well as over a time period, thus presenting the attached biomarker concentration. As for the emulation of the input signal from the photodiode, a laboratory signal generator has been used for this purpose, to test the response of the development setup.

Work Package 5: Clinical validation: analysis and procedures

This work package focused on sample collection and sample preparation. Urine was collected and transported to the laboratory where the cell pellet was separated from the urine (urinary sediment). This fraction is frozen and stored. Patients were recruited as an intend to treat population, i.e. there was a reason for referral to the urologist. So far, 153 samples were collected.

4. Scientific Progress

There is an urgent unmet clinical need to develop highly specific, fast, and ultra-sensitive new technologies for the analyses of different biomarkers to guide personalized therapy in GU cancer patients on time.

In this sense, the GLAM Biosensor will provide a true progress beyond the state of the art in differentiated areas like:

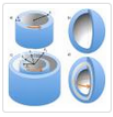
1. The use of photonics for diagnosis in a label-free, fast, sensitive and multiplexed measurement of cancer biomarkers with unprecedented limit of detection (< 10 pM)
2. By the generation of particular recombinant biomarkers and better mAbs with higher affinity and specificity, the detection tools will be improved and consequently sensitivity will increase
3. By turning microring passive resonators into microring lasers, the sensitivity will be improved by several orders of magnitude. These active microrings plus multiplexing and packaging the chips into forefront cartridge device will position GLAM device to a novel standard of diagnosis
4. By providing smart, compact, innovative and integrated prototype system, the pre-clinical and clinical validations will be performed, and the basis for the future product development will be set
5. The most updated clinical trials, in addition to cutting-edge computer analysis tools, including self-learning software, will ensure the most advanced clinical validation of GLAM.

In global terms, GLAM will have significant impact in the early diagnosis of GU cancers. The high specificity and ultra-sensitivity will lead to a considerable reduction in the morbidity associated with prostate and other cancer biopsies; furthermore, the point-of-care format will enable efficient operations in the early diagnosis triage for these cancers. In a similar way, patients with bladder cancer are mostly treated conservatively (i.e. resection of superficial lesions and follow by cystoscopy/cytology). GLAM device will enhance the patient perception of individualized treatment; patients will be treated accordingly to their particular disease profile based on their personal biomarker profile.

Moreover, due to its broad applicability the Glam Biosensor will directly impact on several beneficiaries, starting with the users by providing technology approaches for contributing to the user health, being able to contribute to early diagnostic processes and reduce morbidity and enable better quality of life of the patients omitting more complex diagnostic approaches. There will also be social benefits by providing technology, which is inherently affordable by technology approach allowing future low cost products. Additional benefits also include: economic benefits for the health sector in terms of cost reduction which lead to an improved performance (both due to the diagnosis cost reduction and the time reduction increasing the efficiency of the health sector) are also foreseen.

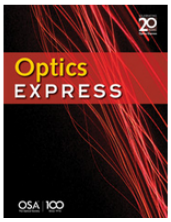
5. Other activities

Article publication by ULB team in Optics Express



Dispersion relations and bending losses of cylindrical and spherical shells, slabs, and slot waveguides

Gregory Kozyreff and Nirmalendu Acharyya



We derive formulas for whispering gallery mode resonances and bending losses in infinite cylindrical dielectric shells and sets of concentric cylindrical shells. The formulas also apply to spherical shells and to sections of bent waveguides. The derivation is based on a Wentzel-Kramers-Brillouin (WKB) treatment of Helmholtz equation and can in principle be extended to any number of concentric shells. A distinctive limit analytically arises in the analysis when two shells are brought at very close distance to one another. In that limit, the two shells act as a slot waveguide. If the two shells are sufficiently apart, we identify a structural resonance between the individual shells, which can either lead to a substantial enhancement or suppression of radiation losses. https://doi.org/10.1364/OE.24.028204

Poster presentation at ETPN 2016 in Heraklion

nanomedicine EUROPEAN TECHNOLOGY PLATFORM | ETPN2016 12-14, October 2016 Heraklion - Greece

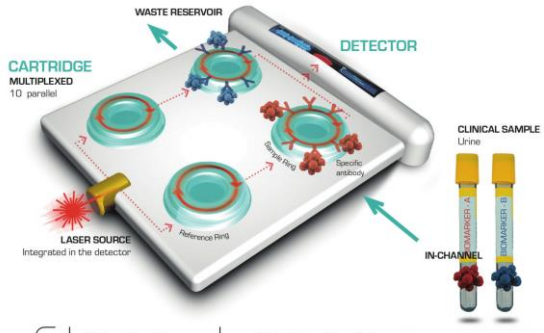
GLAM presented its poster during the ETPN2016 annual event that took place in Heraklion (Greece) from the 12th to the 14th of October 2016. The ETPN is the nanomedicine European Technology Platform and met for their 11th annual event: 3 days meeting the European Nanomedicine community and a great occasion to learn more about GLAM!

18M meeting in Castelldefels hosted by the ICFO & IBEC

On the 3rd and 4th of November 2016, the GLAM consortium met in Castelldefels (Barcelona) at ICFO facilities for the 18M meeting of the project. The meeting was co-organised by the ICFO, the Institute of Photonic Sciences, a centre of research excellence devoted to the science and technology of light, and the IBEC, the Institute for Bioengineering of Catalonia, a leading-edge multidisciplinary research centre in engineering and life sciences.

During the meeting, each work package leader presented an overview of the research activities of the last 6 months. Each point was discussed with the consortium to see how to best meet the objectives. The project execution is going well and the GLAM device is coming closer to its final stage.

New version of the GLAM leaflet



The new GLAM leaflet is available for download! Click here! Discover a first preview of the Glass-Laser Multiplexed Biosensor!

Here is an overview of GLAM's latest achievements:

- GLAM consortium already designed and generated the first prototypes of microring structures Antibodies have already been functionalised to the new microring structures
- Patient recruitment has started to collect urine samples
- Preliminary preclinical proof of principle with soluble biomarkers (10) and its corresponding detecting antibody
- Several aspects related to technical documentations are already implemented by all the consortium partners, which will serve as the regulatory basis for the CE Certification and ISO 13485

GLAM presented during the HEALHIO in Barcelona

HEALTHIO took place from 3-5 May 2017 in Barcelona in Montjuïc venue. HEALTHIO is a fresh, dynamic and interactive event with activities organized by specific areas for innovation in healthcare.

GLAM had an interactive space to present its research activities in the field of cancer diagnosis. LEITAT's team had the opportunity to present the current state of the project to many citizens, doctors and researchers in the field.

Thanks to the visual communication materials, non-experts could understand the basic concepts of the project and were interested in the moment the technology could reach the market.

A 1-minute pitch to understand GLAM technology

LEITAT created a 1-mintue pitch to understand GLAM technology with Dr. Francesc Mitjans. Watch it here: https://vimeo.com/215656621

GLAM project is focused on the design, development and both pre-clinical and clinical characterisation of an innovative, fast, cheap, and ultra-sensitive diagnostic biosensor based on photonic technology.

6. Partners & Contact

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