1. Publishable summary

1.1. Project objectives:

CANDO (www.fp7cando.eu) - **A Cancer Development Monitor.** Some diagnostic applications are extremely demanding, such as those requiring both the identification and concentration determination of extremely low levels of cells in peripheral blood, that to date no such point of care (PoC) diagnostic technology generic or otherwise exists for these. One such application is for the recognition and the concentration measurement of rare circulating tumour cells (CTCs) for early diagnosis staging and monitoring of cancer.

Pancreatic cancer is one such target, and is of strong socio-economic interest as currently it is usually diagnosed at an advanced stage when rapid progression has occurred for widespread disease dissemination and so a 96% chance of death for some 68000 Europeans diagnosed every year. A powerful tool for correct diagnosis and staging of pancreatic cancer would permit not just advances in cancer management, where clinicians could prescribe a suitable early treatment and monitor its progress within theranostics, but also in drug discovery for quick and accurate determination of the effectiveness of new anti-cancer drugs in development tests.

In CanDo, through the integration of various components and sub-systems recently developed in other projects, we will be able to develop a diagnostic platform that will enable accurate and reliable early pancreatic cancer diagnosis, monitoring and prognosis determination based on efficient capture and recognition of CTCs in peripheral blood at unprecedented limits of detection. Specifically it will be based on a disposable cartridge system that combines a powerful cell separation technology; either a combination of inertial microfluidics and high yield sensitive immuno-capture or the GILUPI system, with surface enhanced Raman spectroscopy (SERS) to identify/quantify the CTC and sensitive nanophotonic sensors for nucleic acid analysis from the lysed CTCs for molecular characterization.

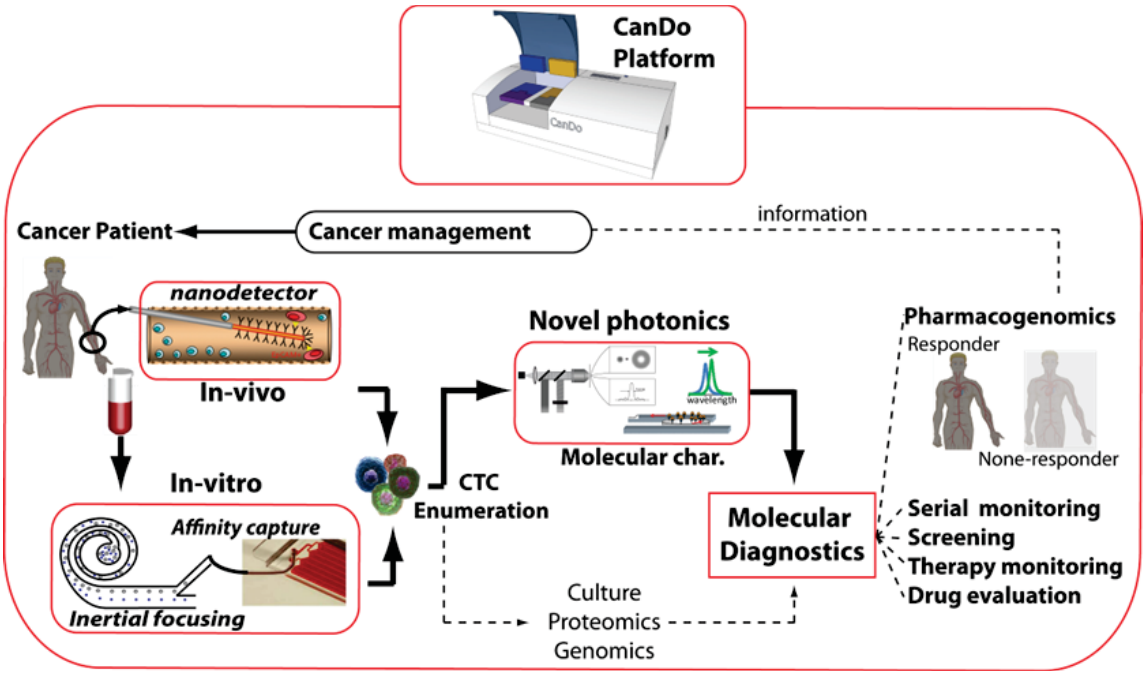


Figure 1.1.1: A schematic of the CanDo platform with indicated components and sub-systems. The platform achieves cancer diagnosis through CTC capture and enumeration (cellular characterization) followed by nucleic acid analysis (molecular characterization). The platform takes whole blood from cancer patient and isolates the CTCs either using a novel in-vivo or in-vitro isolation technology to deliver cell enumeration. The enumerated cells are then further processed for nucleic acid characterization using a label-free photonic sensor array. The information obtained from the CanDo platform can be used for patient management to predict outcomes both good and bad in cancer and to investigate fruitful targets for pharmacological interventions.

1.2. Work done, results to date and the expected final results:

Management: Four project meetings have been successfully organised and all deliverables generated within an acceptable timeframe including the first biannual progress report in M8. All reviewed deliverables except one have been approved. Due administration work was undertaken to produce an amendment to the contract in M6 and a consortium agreement. Following some recommendations from the M9 review the consortium has implemented various measures to meet the demands of such a large complex project with great technical challenges. Future project management and assessment tasks are expected to maintain the successful running of the project leading to a satisfying completion.

Innovation chain definition, specifications, technical assessment and pre-clinical validation: The innovation chain and the end user requirements were evaluated and defined in D2.1. The biological specifications regarding human pancreatic cancer cell lines, cancer cell surface targets and specific antibodies as well as target sequences for mutational analysis were defined in D2.2. The CanDo workflows and technical specifications were defined in the initial MSP (D2.3).

Cartridge I development: Cartridge I has focused on component development of the two parallell CTC isolation tracks (in-vivo and in-vitro) and evaluation of SERS and Raman spectroscopy for label free cell detection.

Cartridge II development: Cartridge II development has focused mostly on developing the individual components (extraction, amplification, detection) as well as providing a first level of integration of 1 or 2 subcomponents.

Platform Development, Integration and Validation: An initial design of the final cancer diagnostic platform capable of executing a complete series of isolation and quantification of circulating tumor cells (CTCs), followed by a molecular analysis of the extracted cells, has been designed. It is worth mentioning that special attention has been paid to the fact of minimal hands-on operation experience, that is, "Sample in/answer out" diagnostic device. A software life cycle-validation procedure has been defined to provide a reliable, robust and error-free operation platform. This will be of paramount importance for testing and pre-clinical validation. In terms of quantification of CTCs, a Raman spectrometer for the identification of CTCs has been defined and developed. In the next months, the platform instrument will be gradually built up from individual component instruments (i.e. valve actuators, heaters, positioning systems, pumping systems…) and then subsystem instruments (i.e. Ring Resonator System, Raman system) will be integrated (Figure 1.2.1). Related to the Raman system, different multivariate approaches for the data evaluation will be analysed so that the redout shows the number of CTC's present in the sample and the accuracy of the analysis.

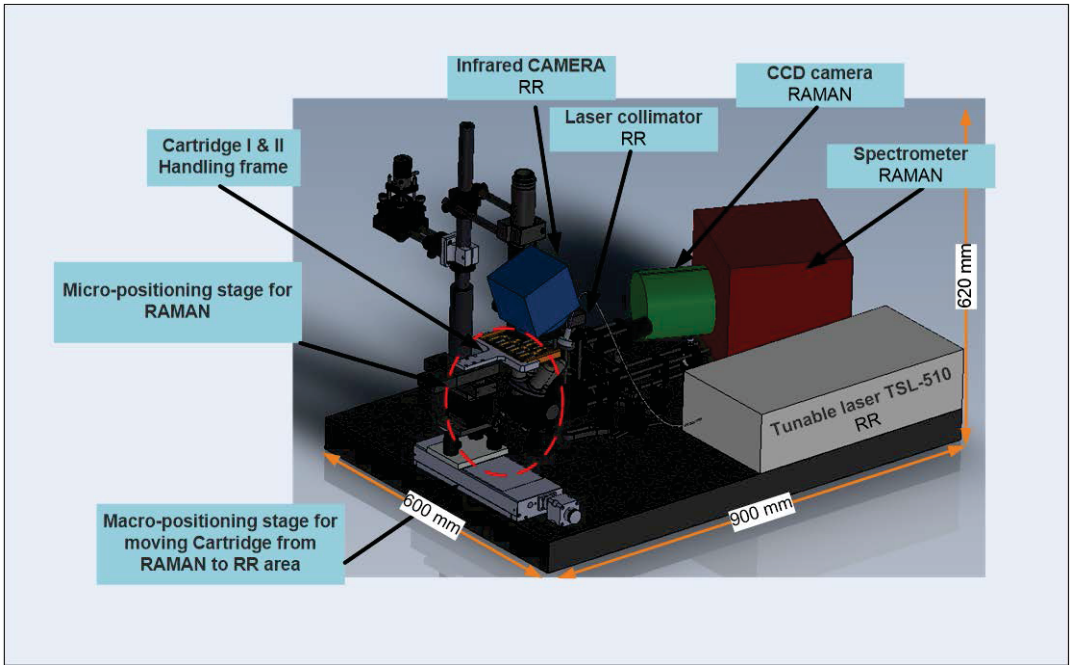


Figure 1.2.1: A 3D design of CanDo platform, including the Raman system and the Ring Resonator (RR) system

Exploitation and dissemination: An interactive webpage, www.fp7cando.eu, has been realised for world-wide knowledge of the activities and results of the project as well as co-ordination between partners. Recently it has been modified to make browsing it a more intuitive and enjoyable experience and content has been updated. Promotional material was generated (leaflets, a poster, a presentation and newsletters) and sent to the CanDo Interest Group (CIG) which includes, amongst many entities, the FP7 Miracle and CTCTrap consortia. Further publicity was generated by presentations of the project at various events and several issued press releases were picked up by technical and non-technical press both on the internet and in newspapers/TV/Radio. An initial plan for using and dissemination knowledge has also been produced and recently updated, and to greatly facilitate the final device integration the distribution of interdisciplinary knowledge is being encouraged through seminars. An initial exploitation plan was drawn up listing foreground of potential commericial interest as well as detailed information on how the foreground could be exploited, especially that of the overall CanDo platform. Recently the plan was updated and includes a Freedom to Operate Report for the platform as part of due-diligence. A collaboration was initiated with the FP7 Miracle consortium with a Non Disclosure Agreement being signed.

1.3. Potential impact and use of results (including the socio-economic impact and the wider societal implications of the project so far):

Through the integration of various components and sub-systems recently developed in other projects CanDo is developing a diagnostic platform that will enable accurate and reliable early pancreatic cancer diagnosis, monitoring and prognosis determination based on efficient capture and recognition of CTCs in peripheral blood at unprecedented limits of detection. Pancreatic cancer is of strong socio-economic interest as currently it is usually diagnosed at an advanced stage when rapid progression has occurred for widespread disease dissemination and so a 96% chance of death for some 68000 Europeans diagnosed every year. A powerful tool for correct diagnosis and staging of pancreatic cancer would permit not just advances in cancer management, where clinicians could prescribe a suitable early treatment and monitor its progress within theranostics, but also in drug discovery for quick and accurate determination of the effectiveness of new anti-cancer drugs in development tests.

To meet these important socio-economic objectives the CanDo platform (Figure 1.2.1) will be based on a disposable cartridge system that combines a powerful cell separation technology; either a combination of inertial microfluidics and high yield sensitive immunocapture or the GILUPI system, with surface enhanced Raman spectroscopy (SERS) to identify/quantify the CTC and sensitive nanophotonic sensors for nucleic acid analysis from the lysed CTCs for molecular characterization. The KEY Innovations expected within the project from realising the novel platform will be:

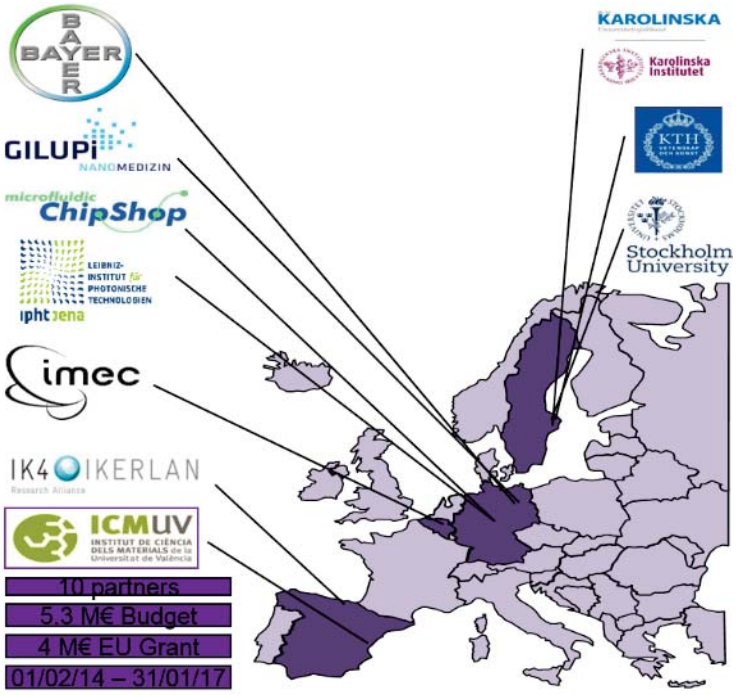
I. An integrated smart cell detection system for sensitive cellular and molecular diagnostics, for the first time in early cancer diagnostics.
II. Sensitive and high throughput isolation of CTCs based on inertial microfluidics1 combined with immunoassay: high-throughput microfluidic procedure to enrich the cell fraction of CTCs from peripheral blood samples by > 4 orders of magnitude, based on selective removal of non-nucleated cells, followed by CTC capture on high-surface microchip with enhanced mixing for optimized surface bound antibody-cell interaction.
III. A novel in-vivo CTC capture method: CellCollector$^{(R)}$ medical device for the increased isolation of rare CTCs direct from the veins of cancer patients.
IV. Structures and membranes featuring novel nanoplasmonic materials for highly efficient cell capture and optimal SERS with the unsurpassed multiplexing capability for simultaneous detection of multiple cancer cell types.
V. Sensitive SERS detection of CTCs without the need of multi fluorescence staining or fixing cells.
VI. The application of an isothermal nucleic amplification method based on Rolling Circle Amplification (RCA) enabling highly multiplexed molecular based cancer diagnostics.
VII. The development of novel ring resonators, Vernier cascade sensors for ultra-sensitive multiplexed, label free, biomolecule recognition.

In addition to the high market potentials of the developed platform in cancer management and drug discovery, the further development and integration of various Key Enabling Technologies within components and

systems across various research fields within CanDo, with its unique combination of multidisciplinary research skills and the four commercially focused partners and their SME networks for technology transfer, will result in:

A. Increased industrial competitiveness, particularly in the 'innovation bridge' SMEs, through greatly strengthened capabilities in systems, as well as innovative products and services in multiple markets.
B. Improvements in innovation capacity and competitiveness of European industry measured through indicators such as an increased number of SMEs and other newcomers taking up novel technologies. These technologies, with their generic nature could lead to other applications based on the modular CanDo systems for other cancers where biomarkers have been identified, as well as in other fields such as food safety and quality, and veterinary diagnostics. The novel component and subsystems, and the development and validation of both within CanDo will also lead to other applications based on them such as within photovoltaics and cancer treatment.

1.4.List of participants and contact details:



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More information can be found on the CanDo website www.fp7cando.eu