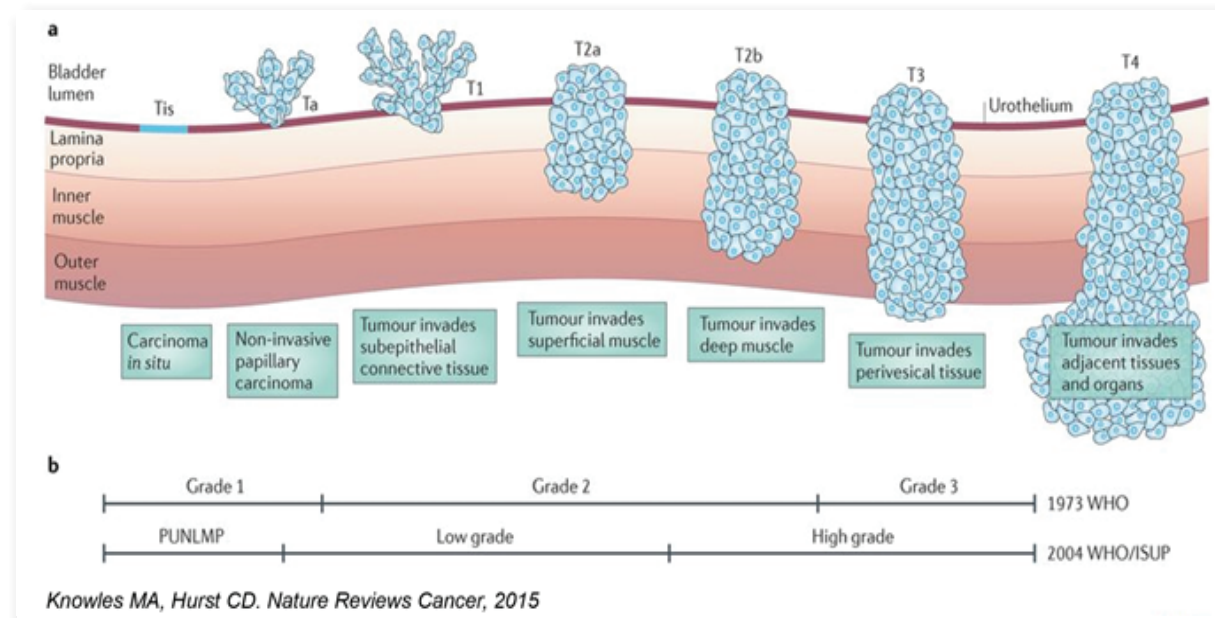


CONCEPT

The need: Bladder cancer (BCa) is characterized by high unmet medical need due to a lack of effective clinical and therapeutic approaches, dating back to early 70's. The annual incidence is 350,000 cases and an estimated 2.7 million people over the world having history of BCa, incurring a cost of tens of thousands Euro/year per patient. The main obstacle in the management of BCa is the incapacity to prevent the relapse and progression of the non-infiltrating aggressive form that is the bladder Carcinoma in situ (Cis/Tis).

The solution: EDIT develops approaches, technologies and visualization strategies for non-invasive detection of pre-neoplastic area and thermoablation of clusters of few cells with high sensitivity and specificity, which have not been attempted so far. To overcome the heterogeneous distribution and poor absorption of the intravesical treatment EDIT will also exploit the ultrasound-mediated sonoporation, a non-invasive approach to distribute gold nanorods (GNRs) to the entire urothelium thus



Most patients with detectable Cis undergo repeated surgeries, each time followed by weekly bladder instillation of adjuvant therapy. However, adjuvant therapy fails in ca 50% of the patients, in part due to the heterogeneous distribution and poor absorption of the intravesical treatment. In patients with multiple Cis or where Cis is progressing and invading the muscle bladder radical cystectomy is the only option. As consequence of technological limitations, patients undergo frequent and endless follow-up and weekly treatments, or radical cystectomy, with a consequent poor quality of life and the highest cost per patient among all cancers.

allowing for the creation of a 3D map of the entire bladder anatomy and recognition of neoplastic modifications. Combining the use of intravesical GNRs modified with selective protein moieties, sonoporation, photoacoustic (PA) and high-frequency ultrasound spectroscopy (US) principles together (PAUS) and algorithms for 3D visualization software, EDIT will provide **2 innovative platforms** for fast, non-invasive and non-ionizing novel technologies for early i) prognosis, and ii) diagnosis and treatment of the aggressive form of bladder Cis, by recognizing fibrotic tissue areas with lateral resolution down to 30 μm .

OBJECTIVES

Early non-invasive prognosis - an innovative application monitoring for the modification of the extracellular matrix, by providing specific effectors, provided by the novel functionalized nanoparticles, to be employed as intravesical source of ultrasound through photoacoustic effect.

Early eradication - locally delivered nanoparticles able to thermal ablating the neoplasia upon near-infrared laser irradiation, allowing to recognize and eradicate cluster of few neoplastic cells <1 mm.

Novel biomarkers - i) characterization of markers that identify pre-conditioning of the extracellular matrix, ii) novel targets for the identification of the in-situ carcinoma, and iii) new ligands for expanding the armamentarium for targeted delivery of gold nanorods, increasing the opportunities for the "bench to bedside", EDIT's translational approach.



THE CONSORTIUM

Acronym: EDIT
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Novel precision technological platforms to promote non-invasive early diagnosis, eradication and prevention of cancer relapse: proof of concept in the bladder carcinoma

EDIT Gatekeepers

- Long term vision** Novel technological platforms for the early detection of neoplastic modifications and early treatment of solid cancers. Proof of concept in preclinical models of bladder cancer, with the set-up validated in swine and ready for clinical application
- Breakthrough** Advanced transformative technology, integrating the use of gold nano-rods, sonoporation, high-resolution sonography and photoacoustic imaging in a unique and novel platform for the 3D visualization of neoplastic modifications up to 30 µm lateral resolution
- Novelty** Novel approach for early and non-invasive prognosis and treatment of solid tumours at level of few cells, based on gold nano-rods as nanoantenna and thermal effectors; 3D visualization platform up to 30 µm lateral resolution
- Foundational** To revolutionize the management of malignant solid tumor, with a proof of concept for bladder cancer
- High-Risk** Ambitious study with high interdisciplinary approach, targeting unmet outcomes in curing solid tumors
- Interdisciplinary** International, multi and inter disciplinary study which could be realised only by the proposed disciplines