

Tumour Markers *Junior Group*

Summary

The main focus of the Tumour Markers Group is the molecular characterisation of bladder cancer, integrating information from high-throughput sources with two main aims: to understand how identified alterations contribute to tumourigenesis and cancer progression; and to translate such information into multiplexed strategies that may improve the clinical management of bladder cancer patients using tissue (outcome prediction) and body fluids (diagnosis and follow-up).

Strategic Goals

- Integrate epigenetic, genetic, transcript and protein tumour profiles characteristic of each step in bladder cancer progression with clinical and pathological endpoints
- Further characterise how targets that we are interested in such as myopodin and KiSS-1, are involved in progression of the disease
- Translate molecular signatures obtained by high-throughput profiling into serum and urine multiplexed biomarkers

Marta Sánchez-Carbayo *Junior Group Leader*



Marta Sánchez-Carbayo was born in Salamanca in 1969. She obtained her Bachelor degree in Pharmacy at the *Universidad de Salamanca* in 1992, and Optics in 1993 at the *Universidad de Barcelona*. From 1994 to 1997 she carried out her FIR residency in Clinical Chemistry at the *Hospital General Universitario*, Alicante, and her PhD simultaneously (1995 – 1998) at the *Universidad Miguel Hernández*, Alicante.

She then continued her work on tumour markers in bladder cancer at the *Hospital Universitario de Salamanca* (1998 – 1999), supported by a Postdoctoral award from the *Asociación Española contra el Cáncer* (AECC). In 1999, she joined C. Cordon-Cardo's laboratory in the Division of Molecular Pathology at the Memorial Sloan-Kettering Cancer Center (MSKCC), New York, USA, with a Postdoctoral Fellowship from the *Fundación Ramón Areces*.

Despite receiving a *Ramón y Cajal Award* in 2001, Marta stayed in New York as Research Associate at MSKCC to further pursue ongoing studies in bladder cancer. She joined the CNIO in December 2005 as Junior Group Leader of the Tumour Markers Group



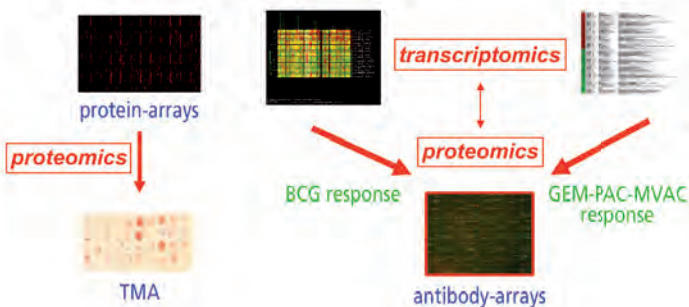
Post-doctoral fellows: Noreli C. Franco (until July), Antonio García (since September), Laura Grau, Esteban Orenes.

Highlights

Body fluid studies

Serum protein profiles using protein arrays showed diagnostic properties for bladder and colon cancer. The protein array approach has identified a panel of immunogenic candidates as potential diagnostic biomarkers, especially for muscle invasive disease. Moreover, the protein expression patterns of dynamin and clusterin in bladder tumours were shown to improve histopathologic staging and clinical outcome prognosis.

A - Defining serum multiplexed bladder cancer biomarkers using proteomic approaches



B - Searching urinary bladder cancer biomarkers using high-throughput approaches

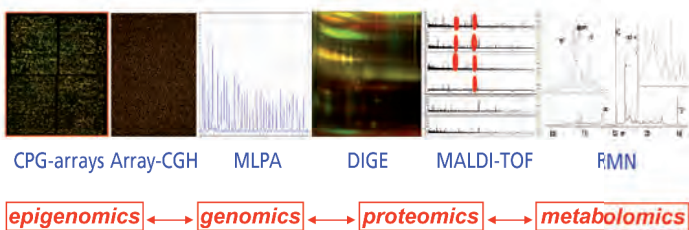


Figure: The general strategy of the Tumour Markers Group aims at integrating high-throughput approaches for the discovery and development of multiplexed biomarkers for bladder cancer: (A) in serum and (B) in urine.

Integrating tumour profiles

In clinical collaborative studies we have recently demonstrated the predictive role of ezrin protein expression patterns in non-maintenance BCG response in patients with high-risk T1G3 tumours. These analyses identified those patients more prone to fail BCG immunotherapy who may require more aggressive therapeutic curative interventions.

Characterisation of genes of interest

In an attempt to characterise the mechanisms by which KiSS-1 is involved in bladder cancer, we have optimised and performed a differential protein expression profiling using iTRAQ-2DLC-MS/MS in human bladder cancer cells transfected with the *KiSS-1* metastasis suppressor gene.

Publications

Babel I, Barderas R, Díaz-Uriarte R, Martínez-Torrecedradora JL, Sánchez-Carbayo M, Casal JI (2009). Identification of tumor-associated autoantigens for the diagnosis of colorectal cancer in serum using high density protein microarrays. *Mol Cell Proteomics* 8, 2382-2395.

Palou J, Algaba F, Vera I, Rodriguez O, Villavicencio H, Sánchez-Carbayo M (2009). Protein expression patterns of ezrin are predictors of progression in T1G3 bladder tumours treated with nonmaintenance bacillus Calmette-Guérin. *Eur Urol* 56, 829-836.

Patents

Sánchez-Carbayo M (2009). A panel of autoantibodies as bladder cancer biomarkers. Reference Number ES200930980.

Sánchez-Carbayo M (2009). Myopodin mutations as bladder cancer biomarkers. Reference Number ES200930981.

Sánchez-Carbayo M (2009). Myopodin methylation as a prognostic and predictive biomarker for bladder cancer. Reference Number ES200931219.