Cellular Control Systems

From cell-cycle checkpoints to RNA polymerase biogenesis

RESEARCH

How does a cell respond to DNA damage?

Our laboratory has a long-standing background in cell-cycle control and genome integrity. Using budding yeast as an amenable eukaryotic model, we investigated how cells prevent chromosome segregation when DNA is damaged or incompletely replicated.

We showed that this response relies on overlapping safeguards rather than a single molecular switch. Three pathways act downstream of the DNA damage response: securin stabilization blocks sister-chromatid separation, while Swe1/Wee1 and Rad53/Chk2 independently inhibit mitotic Cdk1. This revealed a previously unrecognized role for Rad53 that explains why Swe1 can appear dispensable. We also found that the spindle assembly checkpoint provides an additional protective layer when the canonical DNA-damage response is compromised.

Related work identified Cip1 as an S-phase-checkpoint-regulated Cdk1 inhibitor that supports survival during replication stress. We also demonstrated that sufficiently high G1 cyclin activity can trigger DNA replication without the cyclin-CDK activities normally associated with later cell-cycle phases. Together, these studies established our expertise in yeast genetics, molecular cell biology and cellular regulatory networks.

How does a cell build the molecular machines that read its genome?

Every protein-coding nuclear gene depends on RNA polymerase II (Pol II), a 12-subunit molecular machine that transcribes chromosomal DNA into messenger RNA. Before Pol II can function in the nucleus, its components must assemble correctly, pass cellular quality control and reach the chromatin. The pathway that orchestrates this process remains poorly understood.

Why does this matter? Pol II biogenesis is an upstream control point for gene expression: errors in assembly can compromise transcription across the genome. By reconstructing this hidden stage in the life of Pol II, we seek to understand how cells build, transport and safeguard the machinery that converts genomic information into cellular function.

As a visiting scientist at HebAU University, China, I supervise research that combines genetic screens, genome editing, protein-interaction mapping, live-cell imaging and AI-assisted structural analysis to uncover the Pol II assembly machinery. We aim to identify its components, reconstruct their interactions and reveal how assembly factors cooperate in space and time to produce functional polymerases and regulate their access to chromatin.

We have recently reported that the conserved assembly factor Rba50 has a striking modular architecture: a structured module involved in Pol II assembly, a flexible interaction hub and a

nuclear export signal. These findings position Rba50 as a molecular coordinator linking Pol II assembly with the trafficking of its intermediates between cellular compartments.

PROFILE

- Associate Professor (Professor Agregat).
- Project Evaluator for ANEP / AEI Spanish national research funding and evaluation agencies.
- Ramon y Cajal Scientist 2003-2008.
- Research Fellow, Cancer Research UK London Research Institute (now part of the Francis Crick Institute), 2000-2002.
- American Cancer Society Senior Postdoctoral Fellow, 1998-1999.
- Research Fellow, Harvard Medical School, 1996-1999.
- World Health Organization International Agency for Research on Cancer Postdoctoral Fellow, 1996-1997.
- PhD, Universitat Autonoma de Barcelona, 1994.

Career progression of former PhD students:

- Anna Travesa, Postdoctoral Fellow, The Scripps Research Institute, La Jolla.
- Angel Guerra-Moreno, Postdoctoral Fellow, Harvard Medical School.
- Gloria Palou, Postdoctoral Fellow, MRC Clinical Sciences Centre, London.
- Fanli Zeng, Research Associate, Peking University.
- Alba Duch, Postdoctoral Fellow, Universitat Pompeu Fabra, Barcelona.
- Asrar Malik, Postdoctoral Fellow, University of Virginia.
- Roger Palou, Postdoctoral Fellow, University of Montreal.
- Alberto Zurita, Postdoctoral Fellow, Centre for Genomic Regulation, Barcelona.
- Ping Ren, Associate Postdoctoral Fellow, Yale University.
- Nathalie Guibourt, Research Scientist, Celgene Institute of Translational Research Europe.

Lab featured publications:

- Xie D, Wang L, Sun X, Yan Y, Li P, Gao M, Quintana DG, Zeng F (2026). Modular Organization of Rba50 Reveals Distinct Domains for RNAPII Assembly and Interaction Network Formation. FASEB J. 40:e71951.

- Zeng F & Quintana DG (2021). High-Copy Yeast Library Construction and High-Copy Rescue Genetic Screen in Saccharomyces cerevisiae. Methods Mol Biol 2196:77-83.

- Palou R, Palou G, Quintana DG (2017). A role for the spindle assembly checkpoint in the DNA damage response. Curr Genet 63:275.

- Palou G, Palou R, Zeng F, Vashisht AA, Wohlschlegel JA, Quintana DG (2015). Three Different Pathways Prevent Chromosome Segregation in the Presence of DNA Damage or Replication Stress in Budding Yeast. PLoS Genet 11:e1005468.