Oncode Institute

Annual Conference 2025

“Decoding cancer across scales: from genes to tumors”

Abstract Book

6 & 7 November 2025
Koninklijk Instituut voor de Tropen, Amsterdam

Organizing committee:
Kristina Ganzinger, Tineke Lenstra, Hugo Snippert

Oncode Institute

Day 1
November 6
2025

Decoding cancer across scales: from genes to tumors

Scientific Committee: Kristina Ganzinger, Tineke Lenstra, Hugo Snippert

Time	Speaker, Institute & Topic
08.30	**Walk in, registration and coffee**
09.30	**Welcome by Scientific Committee:** Hugo Snippert
	Session I
09.40	**Eduard Batlle** - IRB Barcelona, Spain Plasticity, therapy resistance and immune evasion in metastatic colorectal cancer
10.15	**Paola Scaffidi** - IEO Research, Milan Italy Network-level epigenetic alterations in cancer evolution
10.50	**Break**
11.35	**Ricardo Fernandes** - CAMS Oxford Institute, UK Induced-Proximity Strategies to Modulate Receptor Signalling in Inflammation and Cancer
12.10	**Thijn Brummelkamp** - Netherlands Cancer Institute A Compendium of Genetic Screens to Discover 'Alternative Pathways'
12.45	**Lunch and network**
	Session II
14.00	**Andrea Sottoriva** - Human Technopole, Italy Epigenetic evolution and plasticity in colorectal cancer and the normal gut
14.35	**Susana Minguet Garcia** - University of Freiburg, Germany Harnessing TCR Discoveries for the Next Generation of Immunotherapies
15.10	**Break**
15.55	**Céline Vallot** - Institut Curie, France Epigenomic evolution of breast cancers at single-cell resolution
16.30	**Bill Earnshaw** - University of Edinburgh, Scotland Approaching mitotic chromosome structure from all directions
17.05	**Scientific Committee** Closing Remarks
17.10 - 18:10	**Networking drinks & bites**

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Outsmarting Cancer
Impacting lives

Oncode Institute

Day 2
November 7
2025

Decoding cancer across scales: from genes to tumors

Scientific Committee: Kristina Ganzinger, Tineke Lenstra, Hugo Snippert

Time	Speaker, Institute & Topic
08.30	**Walk in, registration and coffee**
09.30	**Scientific Committee:** Welcome
	Session III - part 2
09.40	Rebecca Fitzgerald - MRC/CRUK, UK Pinning down the molecular origins of esophageal adenocarcinoma to inform earlier detection
10.15	Cédric Blanpain - Université Libre de Bruxelles (ULB), Belgium Mechanisms regulating stem cell plasticity during tumor initiation
10.50	**Break**
11.35	Anna Obenauf - IMP, Austria Unlocking immunity: Decoding and reprogramming the immune-evasive tumor microenvironment
12.10	Omer Dushek - University of Oxford, UK Optimising CAR-T cell sensitivity by engineering extracellular receptor/ligand sizes
12.45	**Lunch and network**
	Session IV
14.00	Danny Sahtoe - Hubrecht Institute, the Netherlands Protein design approaches in chromatin biology
14.35	Luca Giorgetti - Friedrich Miescher Institute, Switzerland Towards a quantitative understanding of enhance-promoter communication
15.10	**Break**
15.55	Titia de Lange - The Rockefeller University, USA Attenuation of ATM signaling by ROS delays replicative senescence at physiological oxygen
16.30	Monika Wolkers - Sanquin, the Netherlands Translation control of T cell effector function
17.05	Scientific Committee Closing Remarks
17.10 - 18:10	**Networking drinks & bites**

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Outsmarting Cancer
Impacting lives

Abstracts oral presentations

Plasticity, therapy resistance and immune evasion in metastatic colorectal cancer

Eduard Batlle

ICREA & Cancer Science Program. Institute for Research in Biomedicine (IRB Barcelona). The Barcelona Institute of Science and Technology (BIST). Barcelona. Spain.

Thursday November 6, 09:40 – 10:15

Only a small proportion of the observed transcriptomic variation between different subclones in a given colorectal cancer (CRC) can be attributed to genetic or epigenetic changes. Instead, intratumor heterogeneity primarily arises from phenotypic plasticity—the ability of cancer cells to adopt different transcriptional states without underlying heritable (epi)genetic alterations. A significant portion of the phenotypic and functional cellular heterogeneity observed in CRC can be traced to the footprints of homeostatic stem cell renewal and differentiation programs expressed by tumor cells. Plasticity is both pervasive and essential for disease progression. Here, I will share our latest discoveries on how tumor cells co-opt different cell states during metastatic dissemination, relapse, outgrowth, and therapy resistance. I will also discuss the impact of tumor cell heterogeneity on immune evasion throughout metastatic evolution.

Network-level epigenetic alterations in cancer evolution

Paola Scaffidi

Cancer Epigenetics, European Institute of Oncology, Milan, Italy

Thursday November 6, 10:15 – 10:50

The complex network of proteins that regulate chromatin and DNA methylation landscapes is often disrupted in cancer. Clonal and subclonal mutations targeting a wide range of molecular functions are frequently observed across cancer types, and emerging evidence suggests that loss of robust epigenetic control promotes both cancer initiation and evolution, independently of context-specific effects. I will discuss how diverse genetic alterations that destabilize the epigenetic regulatory network converge into common phenotypes that confer a selected advantage to the affected cells. I will also discuss the implications of altered network topology and systemic epigenetic disorder for the evolution, vulnerability, and therapeutic resistance of cancers.

Induced-Proximity Strategies to Modulate Receptor Signalling in Inflammation and Cancer

Ricardo Fernandes

CAMS Oxford Institute, UK

Thursday November 6, 11:35 – 12:10

Controlling receptor signalling with precision is essential for reprogramming immune responses and targeting oncogenic pathways. We have developed a modular platform that leverages induced proximity to either inhibit or potentiate receptor activity by recruiting endogenous enzymes. Our core approach, Receptor Inhibition by Phosphatase Recruitment (RIPR), employs bispecific molecules to direct CD45 to immune checkpoints such as PD-1, CTLA-4, and SIRPa, silencing signalling via targeted dephosphorylation. This intracellular strategy bypasses the limitations of traditional checkpoint blockade and synergizes with receptor antagonists.

Extending this framework to receptor tyrosine kinases (RTKs), we mapped phosphatase-receptor interactions across 15 oncogenic RTKs and demonstrated that CD45 recruitment to FLT3 suppresses tumour cell signalling and enhances the efficacy of kinase inhibitors.

In contrast to the phosphatase-recruitment approach, and to enable selective immune suppression, we extended this concept to generate kinase-recruiting bispecifics that act as soluble agonists for inhibitory receptors such as PD-1, BTLA, and CD200R. These molecules potentiate suppressive signalling in defined T cell subsets without Fc engagement or depletion.

Together, these proximity-based strategies uncover new principles of receptor signal integration and provide a conceptual framework for rewiring cellular communication in immune and cancer biology.

A Compendium of Genetic Screens to Discover 'Alternative Pathways

Thijn Brummelkamp

Netherlands Cancer Institute

Thursday November 6, 12:10 – 12:45

Human genes act together in complex networks to perform a myriad of functions. Whereas details maps exist for most biochemical pathways, the wiring of genetic networks in human cells is poorly understood. Using genetics in haploid human cells we have assigned genes to more than a hundred quantitative cellular phenotypes. This approach enables us to identify missing enzymes in cell biology and alternative factors involved in metabolism, cell death and gene regulation.

Epigenetic evolution and plasticity in colorectal cancer and the normal gut

Andrea Sottoriva

Human Technopole, Italy

Thursday November 6, 14:00 – 14:35

"We characterize the epigenetic landscape of colorectal cancer (CRC) and both adjacent and distant normal tissues at single-cell resolution. We used single-nucleus multiomic assays and bulk WGS and identified the most recurrent chromatin alterations affecting promoters and enhancers, including the activation of promoters for ***FOXQ1***, ***TOP1***, ***PTCH1***, and ***PLCG1***, and inactivation of promoters for ***TP53***, ***SMAD3***, and ***TSC2***. The recurrence of these SCAAs was significantly higher than that of many genetic driver mutations. An analysis of genome-wide chromatin accessibility in tumor cells at transcription factor (TF) binding sites revealed increased accessibility associated with the *TCF7/LEF1* family, homeobox TFs (*HOX*, *FOX, SOX* families), and *SNAI1/2/3* TFs. A comparison of normal epithelial cells adjacent to the tumor core versus distal normal epithelial cells revealed a subset of chromatin changes in cancer-related genes. Epigenetic footprints affecting extracellular matrix remodeling and antigen presentation were detected in stromal cells adjacent to tumors, compared to stroma within normal colon tissue. Hence, recurrent chromatin alterations in most CRC samples represents stable, heritable events. Alterations of chromatin accessibility in normal cells adjacent to tumors suggest a spatially dependent epigenetic shift influenced by the tumor microenvironment.

Harnessing TCR Discoveries for the Next Generation of Immunotherapies

Susana Minguet Garcia

University of Freiburg, Germany

Thursday November 6, 14:35 – 15:10

Recent advances in synthetic immunology and CAR T cell engineering have highlighted the critical importance of signaling diversity for optimizing anti-tumor responses. Our work outlines the design of innovative cell-based cancer immunotherapies rooted in a molecular understanding of T cell activation via the T cell receptor complex (TCR–CD3). I will discuss how modulating receptor signaling interfaces and precisely recruiting kinases and adaptors can advance both fundamental immunology and translational therapies. Key noncanonical interactions between specific components of the TCR–CD3 complex and the Src-kinase Lck fine-tune T cell activation; when implemented in chimeric antigen receptors (CARs), these mechanisms improved in vivo tumor control and reduced T cell exhaustion. Supporting our rational design of next-generation CAR T cells, we demonstrated that harnessing CD3 chain diversity, rather than simply increasing signaling strength, enabled the generation of CAR T cells with enhanced anti-tumor efficacy and safety profiles.

Epigenomic evolution of breast cancers at single-cell resolution

Céline Vallot

Institut Curie, France

Thursday November 6, 15:55 – 16:30

The dynamic nature of chromatin and transcriptional features are expected to participate to tumor evolution. Our group focuses on the study of the dynamics of histone modifications in cancer cells upon cancer treatment as well as during the initial steps of tumorigenesis. We develop experimental and computational approaches to map histone marks at single-cell resolution, enabling the investigation of the dynamics of chromatin marks in model systems and human samples. We have for example combined single-cell epigenomic and transcriptomic approaches to lineage tracing strategies to reveal the initial epigenomic events driving tolerance to chemotherapy in triple-negative breast cancer. We have shown that the repressive histone mark H3K27me3 is a lock to the activation of a drug-persistent expression program in breast cancers. Using demethylase inhibitor in combination to chemotherapy, we improve the response rate and delay recurrence both in vitro and in vivo. We also study mechanisms of cell plasticity in early breast tumorigenesis *in vivo*. We have recently mapped state transitions during Brca1-tumorigenesis in the mouse. We discovered that luminal progenitor cells undergo a major epigenomic disruption prior to a partial epithelial to mesenchymal transition at the onset of tumorigenesis.

Approaching mitotic chromosome structure from all directions

Bill Earnshaw

University of Edinburgh, Scotland

Thursday November 6, 16:30 – 17:05

Attempts to understand how the DNA is packaged in mitotic chromosomes are confounded by the huge size of the DNA, the incredible chromatin density in mitotic chromosomes and the complexity of the machinery that does the DNA packaging. We study this problem by combining chemical genetics, Hi-C genomic analysis, polymer modelling, light and electron microscopy and proteomics. In our system, an entire cell population of chicken DT40 lymphocytes enters mitosis with near perfect synchrony within 2 to 3 minutes of release of a G_2 phase arrest. This allows us to "kinetically section" the process and perform biochemical and structural analyses with minute-by-minute resolution. The cells can be engineered so that chromosome formation is directed by single SMC complexes: cohesin, condensin I or condensin II. Our latest models reveal that chromosomes are a disorderly helix of loops created by the SMC complexes. Condensin II drives the formation of cylindrical chromosomes but is restrained from achieving its ideal state by residual cohesive cohesin. Our electron microscopy analysis in human cells reveals that nucleosomes achieve a near millimolar concentration in mitotic chromosomes. The data from our electron microscopy and modelling are most consistent with chromosome formation involving a combination of looping by SMC complexes and chromatin phase separation. However, the chromatin concentration in chromosomes is much higher than the concentration of nucleosomes in phase-separated droplets in vitro. The mechanism responsible for this compaction of the chromatin is unknown and we have recently obtained evidence inconsistent with all previous models for how the compaction is achieved. Preliminary evidence suggests that a preference of condensin I for G:C_rich DNA may drive a radial organisation where A:T-rich DNA is preferentially located towards the chromosome periphery. Despite over 140 years of study, the essential mysteries of miotic chromosome formation remain elusive.

Pinning down the molecular origins of esophageal adenocarcinoma to inform earlier detection

Rebecca Fitzgerald

MRC/CRUK, UK

Friday November 7, 09:40 – 10:15

Cancer medicine is undergoing a radical shift away from a reactive approach in patients presenting with symptomatic disease towards a more proactive approach aimed at early diagnosis, including at the pre-cancerous stage. Oesophageal adenocarcinoma develops gradually from the pre-malignant condition Barrett's oesophagus which presents an opportunity to radically improve outcomes from this highly aggressive cancer. Work to unravel the: underlying risk factors; the cell of origin of this disease; and the molecular landscape of Barrett's samples over time and space, in patients with different outcomes, is shedding light on the disease pathogenesis. I will discuss how our improved understanding of the disease can be used to develop novel approaches to risk-based population screening and personalised prevention.

Mechanisms regulating stem cell plasticity during tumor initiation

Cédric Blanpain

Université Libre de Bruxelles (ULB), Belgium

Friday November 7, 10:15 – 10:50

Glandular epithelia, such as the mammary gland and the prostate, develop from multipotent stem cells (SCs), which are replaced in adult life by different types of lineage-restricted basal and luminal unipotent SCs. Upon oncogenic hits, the lineage restricted SCs can re-activate multipotent features reminiscent of the embryonic progenitors. However, the molecular mechanisms regulating cell plasticity and oncogene-induced reprograming during mammary gland and prostate tumorigenesis are poorly understood. I will present new studies combining lineage tracing, clonal analysis, single cell RNA sequencing, chromatin profiling as well as in vitro and in vivo functional experiments investigate the cellular and molecular mechanisms regulating cell fate and plasticity during the early stage of mammary gland and prostate tumor initiation. Understanding how the mechanisms regulating SC fate and plasticity are corrupted during tumor initiation and progression will have important implications for cancer prevention and therapy.

Unlocking immunity: Decoding and reprogramming the immune-evasive tumor microenvironment

Anna Obenauf

IMP, Austria

Friday November 7, 11:35 – 12:10

Targeted therapies and immunotherapies have transformed the clinical care of patients with metastatic cancer. By optimizing treatment with combinations of different therapies, a cure appears within reach for many cancers. However, achieving this goal will require more detailed knowledge of the mechanisms of therapy resistance and immune evasion and, importantly, of the impact of therapies on tumor evolution, which may promote or prevent subsequent therapy responses. The vision of my lab is to build and exploit this knowledge to identify rational combinations of existing and emerging therapies by understanding the complex and dynamic biology of cancer cells and the tumor microenvironment in all phases of therapy. In this presentation I will focus on how the tumor microenvironment shapes anti-tumor immune responses, how cancer cells establish an immune-evasive tumor microenvironment and on our efforts to understand how to induce an immune-permissive state in cancer cells.

Optimising CAR-T cell sensitivity by engineering extracellular receptor/ligand sizes

Omer Dushek

University of Oxford, UK

Friday November 7, 12:10 – 12:45

Chimeric antigen receptor (CAR)-T cells exhibit low antigen sensitivity, which restricts their therapeutic efficacy and leads to patient relapses when cancer cells downregulate antigen expression. Despite the pressing need to overcome this limitation, the underlying mechanisms remain poorly understood. Here, we demonstrate that enhancing CAR sensitivity to match the sensitivity of the T-cell receptor (TCR) can be achieved by engineering matched extracellular sizes of CAR/antigen and CD2/CD58 complexes. We find that different CAR/antigen sizes, which are generated by different CAR architectures and different target antigens, require a different CD2/CD58 size to optimise sensitivity. This extracellular size-matching improves antigen engagement and co-localisation of CAR/antigen and CD2/CD58 complexes. We also find that size-matching controls co-inhibition of CARs by PD-1/PD-L1. These findings highlight the importance of size-matching for signal integration by surface receptors and offers a new approach to tune CAR-T cell sensitivity by matching or mismatching extracellular sizes.

Protein design approaches in chromatin biology

Danny Sahtoe

Hubrecht Institute, the Netherlands

Friday November 7, 14:00 – 14:35

A large proportion of natural proteins contain regions do not fold into stable structures but rather exist in an ensemble of conformations that rapidly exchange. Such regions have traditionally been understudied but play key roles in processes such as cell signaling, liquid-liquid phase separation and gene regulation. We present a protein design approach to *de novo* design proteins that can capture disordered regions and interrogate their function. Using our approach we design proteins that can interact with factors involved in chromatin biology, and proteins that can control the relative orientation of individual domains in multidomain proteins as a way of controlling function. We anticipate that these designs can be used to study fundamental processes in molecular biology.

Towards a quantitative understanding of enhance-promoter communication

Luca Giorgetti

Friedrich Miescher Institute, Switzerland

Friday November 7, 14:35 – 15:10

Control of gene expression in mammalian cells relies on many thousand distal enhancer sequences, which can be located at large genomic distances from their target promoters. Genetic variation within enhancers is a major driver of evolution, but it is also cause to developmental disorders, oncogenic transformation, and complex human disease. Yet despite their central role in gene regulation in health and disease, the principles by which enhancers select and control their target genes remain largely unknown. What are the molecular and biophysical mechanisms that transmit regulatory information from an enhancer to a promoter? What is the role of chromosome structure and physical proximity between distal regulatory sequences? How do the position, number, and arrangement of enhancers determine promoter expression levels within a genomic region and its variability in individual cells? My group addresses these and other fundamental open questions using experimental and theoretical approaches at the interface of molecular biology, genome engineering and biophysics, which enable the quantitative measurement of molecular processes and the identification of emerging regulatory principles.

Attenuation of ATM signaling by ROS delays replicative senescence at physiological oxygen

Titia de Lange

The Rockefeller University, USA

Friday November 7, 15:55 – 16:30

Replicative senescence, a powerful tumor suppressor pathway, occurs when a few critically-short telomeres activate the DNA damage response (DDR). We show that ATM is the sole DDR kinase responsible for the induction and maintenance of replicative senescence and that ATM inhibition can induce normal cell divisions in senescent cells. Compared to non-physiological normoxia (~20% oxygen), cells grown at physiological (3%) oxygen were more tolerant to critically-short telomeres, explaining their extended replicative life-span. We show that this tolerance is due to attenuation of the ATM response to double-strand breaks (DSBs) and unprotected telomeres. Our data indicate that the reduced ATM response to DSBs at 3% oxygen is due to increased ROS, which induces disulfide-bridges in ATM, generating crosslinked ATM dimers that do not respond to DSBs. This regulation of cellular life-span through attenuation of ATM at physiological oxygen has implications for tumor suppression through telomere shortening.

Translation control of T cell effector function

Monika Wolkers

Sanquin, The Netherlands

Friday November 7, 16:30 – 17:00