DIPARTIMENTO DI FARMACIA E BIOTECNOLOGIE

# AVVISO DI SEMINARIO

Il giorno **venerdì 14 Dicembre 2018**
alle ore **14:30**,
presso l'Aula A
ex-farmacologia via Irnerio 48

il **Dr. Andrew Holding, PhD**
Cancer Research UK, University of Cambridge, United Kingdom
(ospite Dott. Federico Manuel Giorgi)

terrà un seminario dal titolo:

## REPROGRAMMING LUMINAL BREAST CANCER: EXPERIMENTAL & COMPUTATIONAL INFERENCE OF ESTROGEN RECEPTOR INTERACTIONS TO DERIVE COMBINATORIAL DRUG TARGETS

Colleghi e studenti sono cordialmente invitati

*Commissione Ricerca e Attività Correlate - FaBiT*

## ABSTRACT

Combinations of targeted therapies are proposed as the solution to maximise effectiveness and minimise toxicity in the treatment of cancer.

Simultaneously, recent studies have identified several Estrogen Receptor (ER) cofactors, the key driver in 70% of breast cancer cases, as potential novel therapeutic targets that bypass resistance to conventional therapies.

However, the sheer number of potential combinations and the importance of the order in which the drugs are used means it is not possible to trail all of potential therapies within the clinic.

To resolve this challenge, Andrew's team has developed state-of-the-art machine learning, proteomic, and genomic methods to enable them to study the Estrogen Receptor with unprecedented detail:

1) VULCAN applies machine learning to patient data to predict the activity of proteins within ER complex and discovered the direct interaction of ER-GRHL2, a key transcription factor governing the epithelial–mesenchymal transition.
2) qPLEX-RIME enabled the direct and quantitative measurement of changes in the ER interactome, leading to the discovery of ZMIZ1 within the ER complex and its role as a coactivator.
3) Parallel-factor ChIP-seq enabled the precise monitoring of ER binding genome-wide, enabling him to rewrite 20 years of dogma of how the ER responds to its key ligand to drive the growth of cancer.

Together, these tools provide the solution. By integrating the output of these technologies, Andrew can generate detailed hierarchical models of the interactions that programme ER signalling axis. These models predict the transcriptional response to potential therapeutic interactions, and thereby will help design a new generation of therapies that bypass resistance, increase therapeutic response, and minimise toxicity.

http://andrewholding.com/cv/

## BIOGRAPHICAL SKETCH

Dr Andrew Holding is a Senior Research Associate at Cancer Research UK's Cambridge Institute and Fellow of Downing College, Cambridge University, United Kingdom.

Andrew studied chemistry at the University of Oxford before he went on to apply these skills to investigate how life works at a molecular level. During his PhD at the University of Cambridge, he focused on how nature makes the antibiotics we use to treat antibiotic-resistant infections including MRSA. In 2009, he moved to the MRC Laboratory of Molecular Biology as a Career Development Fellow; here he investigated how the machinery within cells interacts to enable basic processes including the replication of DNA. Then in 2013, Andrew moved to the Cambridge Institute where he built on these experiences to lead a team characterising the molecular interactions that drive cancer.

In 2018, Andrew was awarded a Turing Fellowship at the Alan Turing Institute to support the application of deep-learning strategies to model the biological systems he studies. These models will predict new therapies that bypass resistance and minimise side-effects in patients.