

## BCH 252 Seminar Series



**Dr. Francesca Mattioli, Group Leader,  
Hubrecht Institute, Netherlands**

**Seminar Title: “Mechanism of CAF-1  
dependent nucleosome assembly during DNA  
replication”**

**Abstract:** Chromatin organization regulates genes expression and cell fate. Chromatin organization must be accurately inherited during cell division to control development and tissue homeostasis. Chromatin is replicated in tight conjunction with DNA in S phase of the cell cycle. A key regulator of chromatin replication is the Chromatin Assembly Factor-1 (CAF-1) complex. CAF-1 is recruited by PCNA to assemble chromatin at sites of DNA synthesis. PCNA's primary function is to tether DNA polymerases to DNA to increase their processivity. As such, PCNA links DNA synthesis to chromatin assembly. However, whether CAF-1 and DNA polymerases directly share PCNA, and whether this coupling mechanism is equally controlled on the two daughter strands remains unclear. Here, we use comprehensive biochemical reconstitutions with yeast proteins to elucidate how CAF-1 interacts with PCNA and how this crosstalks to DNA replication. We find that CAF-1 needs to simultaneously bind PCNA and DNA to be stably recruited. Two CAF-1 complexes bind to PCNA and this is important for the nucleosome assembly activity of CAF-1. By monitoring the effect of CAF-1 on the activity of the two replicative DNA polymerases, we find that CAF-1 can share PCNA with DNA polymerase delta (the lagging strand polymerase), but not with DNA polymerase epsilon (the leading strand polymerase). This suggests an unexpected differential regulation of this process on the two daughter strands.

Ongoing work is focused on unraveling the molecular basis of these crosstalks and its functional implications in human cells.

**ZOOM Link:** <https://ucr.zoom.us/j/97233953239?pwd=U2w1VWdtcDI4WW8rRXdTUVp2WWp4dz09>

**Meeting ID:** 972 3395 3239

**Passcode:** 609143

**Tuesday, February 15th, 2022  
12:00 p.m. - 12:50 p.m.**

**Host: Dr. Sihem Cheloufi**