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HSP110 Contributes to DNA Repair in Colorectal Cancer Cells Exposed to Genotoxic Chemotherapeutic Drugs

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Colorectal cancers (CRC) is one of the major causes of death in a westernized community where the 5-year survival rate is around 65%. New treatments are being investigated worldwide including through the inhibition of a number of chaperones of the Heat Shock Proteins (HSP) family. In 2011, a mutation was discovered for one such heat shock protein, HSP110, in colorectal cancer with microsatellite instability (MSI). Patients bearing this mutation have a reduced expression of HSP110 and an excellent response to adjuvant chemotherapy, with a 5-year disease free survival rate over 90%. Interestingly, the absence of HSP110 was not compensated by the expression of other heat shock proteins. In the present study, we show that HSP110 translocates to the nucleus after a genotoxic insult. There, it interacts with the Ku heterodimer and contributes to efficient DNA repair through the non-homologous end joining pathway. The inhibition of DNA-PK in colorectal cancer cells expressing HSP110 is enough to restore the sensitivity of these cells to oxaliplatin. Finally, our study confirms that HSP110 might be a good therapeutic target for the treatment of colorectal cancer using genotoxic drugs.

Biography:

Sebastien Causse carried out his PhD at the Ecole Normale Superieure in Paris, France, under the supervision of Dr. Xavier Darzacq. There he worked on the dynamics of transcription by RNA Polymerase 2. He then went on to work in the team of Dr. Carmen Garrido at the University of Burgundy in Dijon, France. He worked on HSP110 and its role in the resistance of colorectal cancer to chemotherapy. He is now working with both the teams of Dr. Garrido and Pr. Ana Maria Cuervo (at the Albert Einstein College of Medicine, New York) on HSP110 and its involvement in autophagy.