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Autore	MERIGLIANO, CHIARA
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Sommario	Cellular responses to DNA damage are based on signal-transduction pathways involving phosphorylation-dephosphorylation events. Recent literature has demonstrated that protein serine/threonine phosphatases have important functions in DNA damage response (DDR). In particular growing evidence indicate that the protein phosphatase 2A (PP2A) plays a crucial role in genome stability maintenance, acts as tumor suppressor and is mutated in some cancer types. However current knowledge on the mechanisms and the pathways linking PP2A to DDR is still rudimentary. Although most of the roles of PP2A are evolutionarily conserved, there are at present very few data suggesting an involvement of Drosophila PP2A in DNA repair. In the course of a screening aimed at identifying new Drosophila genes involved in the maintenance of genome stability we found an allele of twins (tws) gene, encoding the regulatory PP2A B subunit, that caused frequent chromosome aberrations (CABs), suggesting that also in Drosophila this phosphatase is involved in DNA repair. We observed that all previously identified alleles at the tws locus also caused CABs and high frequency of spontaneous -H2Av foci. Moreover tws mutations determined -H2Av foci persistence in irradiated brain cells, indicating that Tws promotes foci regression by dephosphorylating -H2Av. We also demonstrated

	that mutants in the Pp4-19C gene, that encodes the PP4 catalytic subunit, affected -H2Av foci dissolution but not exhibited CABs suggesting that impaired foci regression is not sufficient to cause CABs. PP2A and PP4 are also involved in the G2/M checkpoint. In irradiated tws mutant brains the mitotic index (MI) did not drop at 15 minutes (min) as in control cells, but remained similar to that of non-irradiated controls without significant variations over time. In contrast in Pp4-19C mutant cells MI dropped at 15 min after irradiation but the recovery was significantly delayed. These data indicate that PP2A and PP4 are both implicated in the G2/M checkpoint although with different roles. To better understand the origin of CABs in tws mutants we tried to individuate Tws substrates by cytological examination of double mutants carrying tws mutation and mutations in genes involved in DDR pathway. This analysis revealed that mutations in the ATM-coding gene tefu and mutations in ku70 gene, encoding a component of NHEJ system, are both perfectly epistatic to tws mutations. From these data we deduced that Tws controls genome integrity through a pathway in which Ku70 is first phosphorylated by ATM and then dephosphorylated by Tws (that perhaps dephosphorylates also ATM itself) to allow DNA repair. Therefore, in tws mutants CABs are induced by the hyperphosphorylation status of Ku70.
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