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Kristijan Ramadan, Ivan Dikic

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dysfunction accelerated ageing various degenerative diseases or cancer The sole function of DDR is to recognize diverse DNA lesions signal their presence activate cell cycle arrest and finally recruit specific DNA repair proteins to fix the DNA damage and thus prevent genomic instability DDR is composed of hundreds of spatiotemporally regulated and interconnected proteins which are able to promptly respond to various DNA lesions So it is not surprising that mutations in genes encoding various DDR proteins cause embryonic lethality malignancies neurodegenerative diseases and premature ageing The importance of DDR for cell survival and genome stability is unquestionable but how the sophisticated network of hundreds of different DDR proteins is spatiotemporally coordinated is far from being understood In the last ten years ubiquitin ubiquitination and the ubiquitin relative SUMO sumoylation have emerged as essential posttranslational modifications that regulate DDR Beside a plethora of ubigutin and sumo E1 activating enzymes E2 conjugating enzymes E3 ligases and ubiquitin sumo proteases involved in ubiquitination and sumoylation the complexity of ubiqutin and sumo systems is additionally increased by the fact that both ubiquitin and sumo can form a variety of different chains on substrates which govern the substrate fate such as its interaction with other proteins changing its enzymatic activity or promoting substrate degradation The importance of ubiquitin SUMO systems in the orchestration of DDR is best illustrated in patients with mutations in E3 ubiquitin ligases BRCA1 or RNF168 BRCA1 is essential for proper function of DDR and its mutations lead to triple negative breast and ovarian cancers RNF168 is an E3 ubiquitin ligase which creates the ubiquitin docking platform for recruitment of different DNA damage signalling and repair proteins at sites of DNA lesion and its mutations cause RIDDLE syndrome characterized by radiosensitivity immunodeficiency and learning disability In addition recently discovered the ubiquitin receptor protein SPRTN is part of the DNA replication machinery and its mutations cause early onset hepatocellular carcinoma and premature ageing in humans Despite more than 700 different enzymes directly involved in ubiquitination and sumoylation processes only few of them are known to play a role in DDR Therefore we feel that the role of ubiquitin and the ubiquitin related SUMO in DDR is far from being understood and that this is the emerging field that will hugely expand in the next decade due to the rapid development of a new generation of technologies which will allow us a more robust and precise analyses of human genome transcriptome and proteome In this Research Topic we provide a comprehensive overview of our current understanding of ubiquitin and SUMO pathways in all aspects of DDR from DNA replication to different DNA repair pathways and demonstrate how alterations in these pathways cause genomic instability that is linked to degenerative diseases cancer and pathological ageing **Petroleum Times** ,1967 Hydrocarbon Processing & Petroleum Refiner Chemical Week ,1969 Some vols include Buyer s guide **Research Centers Directory** ,1960-07 **MEED.** ,1990 ,2005 Commerce Today: October 19, 1970 - Vol. 1 - No. 1, 1970 Lok Sabha Debates India, Parliament, House of the People, India. Parliament. Lok Sabha, 1968

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