# ROLE OF EXOSOMES IN THE STUDY OF IONIZING RADIATION ASSOCIATED TO HUMAN HEALTH RISKS

*Ph.D. Student:* Flavia Tortolici / *Supervisor:* Prof. Stefano Rufini

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All life on earth is continually exposed to low level ionizing radiation (IR) stresses. Much harsher and more threatening radiation environments existed during the early years of our planet. On average, 80% of the annual dose of background radiation that a person receives is due to naturally occurring terrestrial and cosmic radiation sources. Today the use of artificially produced radiation is important for both therapeutic and industrial purposes.

The interaction of the IR with the living material implies a deposition of energy able to excite/ionize the atoms of macromolecules; in biological tissue this can lead to cells damage with a morphological and functional alteration.

Many studies show that *in vitro* cells, not exposed directly to IR, present genetic and epigenetic changes that occur in nearby cells directly-hit, due to intercellular communication or soluble factors released by irradiated cells: this type of indirect effect was named "bystander effect"(BE).

Recent studies have shown that the BE is an event that happens also *in vivo*, and implicates the need for reevaluation of approaches currently used to estimate radiation-associated health risks. Recently great emphasis was given to the key role played in intercellular communication by membrane vesicle trafficking serving as vehicles for proteins, lipids, and RNA. A particular vesicle type, the exosomes (50-100 nm in diameter) secreted by many cell types, are released when multivesicular bodies fuse with the plasma membrane. Exosomes can be detected both *in vitro*, in culture medium, and *in vivo* in different body fluids (blood, urine, saliva etc…); because they show a stable and tissue specific proteomic and RNA hallmark profiles, may be considered important biomarkers.

My PhD project aims to achieve two main targets: i) to characterize the role of exosomes in the BE transmission after low and high doses irradiation *in vitro* different cellular models (keratinocytes, fibroblasts and neuroblastoma cells); ii) to understand how exosomes are involved in the messages exchange between irradiated and non-irradiated tissues *in vivo* organism.

A better understanding of these mechanisms may help to minimize radiation effects induced in different scenarios such as environmental exposures, radioactive emergencies and therapeutic/diagnostic treatments.