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Involvement of extracellular proteases ADAM17 and ADAM10 in germ cell apoptosis induced by etoposide

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We have recently determined that the extracellular protease TACE/ADAM17 is involved in physiological (constitutive) germ cell apoptosis. The mechanism underlying apoptosis induction in cancer cells has been studied in different cell types, but it is not known whether the same factors participate in viable germ cells. Since testicular cancer primarily affects young males, we used pubertal rats (21 days old) as a model to determine whether etoposide induces apoptosis through TACE/ADAM17 upregulation, akin to physiological process. Germ cell apoptosis induced by DNA damage was associated with an increase in protein levels and cell surface localization of TACE/ADAM17 and ADAM10. On the contrary, apoptosis of germ cells induced by heat stress, another cell death stimulus, did not change levels or localization of these proteins. Pharmacological *in vivo* inhibition of TACE/ADAM17 and ADAM10 prevents etoposide-induced germ cell apoptosis. Gleevec (STI571) a pharmacological inhibitor of p73, a master gene controlling apoptosis induced by etoposide, prevented the increase of TACE/ADAM17 levels. In vitro, using a germ cell line model, etoposide was also able to induce up regulation of ADAM10 and TACE/ADAM17. Pharmacological and genetic inhibition of both enzymes (knockdown) prevented apoptosis induced by etoposide. Our results strongly suggest that TACE/ADAM17 participates in apoptosis of male germ cells induced by DNA damage. Therefore, we have showed a new and a previously unanticipated element in the mechanism of apoptosis induced by etoposide.

Biography

Ricardo Moreno has completed his Ph.D at the age of 26 years from Pontificia Universidad Católica de Chile and postdoctoral studies from Oregon Regional Primate Research Center. He is associate Professor at the Physiology Department (Biological Sciences Faculty, Pontifical Catholic University of Chile). He has published more than 35 papers in reputed journals and serving as associate or editorial board member in several journals.