Metallothionein colon crypt immuno-positivity as a rapid in vivo essay for drug efficacy studies

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Metallothionein immune positivity indices are considered as representative of crypt stem cell mutations. The frequency and size of MT-immunopositive foci, as well as the total number of MT-immunopositive crypts were assessed here in a short term in vivo assay. Drug efficacy was tested on early mutated crypts in colon of Balb-c mice 30 days after induction with a single dose of the mutagen dimethylhydrazine. The different drugs used (MS 275, vioxx, 5-fluorouracil, aminophylline, 5-azadeoxycytine) affected the metallothionein-immunopositive crypt frequency according to their predicted efficacy on this specific model of mouse colon carcinogenesis. This preliminary validation study of metallothionein-immunopositive crypt frequency strengthens the evidence that metallothionein immunopositivity indices could be used as short-term markers to assess the capability of different pro-drugs to counteract crypt invasion and clonal expansion of mutated stem cell progeny. This rapid in vivo test (30 days) based on metallothionein immunopositivity indices can be assayed in paraffin-fixed tissue sections and has been validated against the glucose 6 phosphate dehydrogenase assay. To quantify metallothionein immunopositivity indices, a novel fast analysis protocol based on the Zeiss Axiovision software for image processing was devised.

Biography
Domenico Lazzaro has obtained his Medical Doctor degree from The 1st University of Rome “la Sapienza” and completed his Post-Doctoral studies from the E.M.B.L. (European Molecula Biology Laboratory) Heidelberg Germany. He continued his Postdoctoral work first at the N.I.H. (Bethesda MD) in the L.T.C.B. laboratory in the molecular section leaded by F. Wong-Staal and in the Microbiology Department of Columbia University (N.Y.N.Y). He was for almost 20 years laboratory head in IRBM Merck Research Laboratories Rome, until 2009. Now he is back in an academic environment. He has published more than 40 papers in reputed journals.

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