Radiation-Induced Heritable Minisatellite Mutations among Children of Estonian Chernobyl Cleanup Workers

Kiuru A[1], Luokkamäki M[1], Makkonen K[1], Vasara R[2], Servomaa K[2],
Rytömaa T[3], Veidebaum T[4], Tekkel M[4], Rahu M[5] and Mustonen R[1]
[1]STUK-Radiation and Nuclear Safety Authority, Radiobiology laboratory, Helsinki, Finland
[2]North Savo Regional Environment Center, Kuopio, Finland
[3]University of Kuopio, Department of Environmental Sciences, Kuopio, Finland
[4]Estonian Institute of Experimental and Clinical Medicine, Tallinn, Estonia
[5]Estonian Cancer Registry, Hiiu 42, EE-0016 Tallinn, Estonia

Analysis of germline mutations in humans exposed to ionizing radiation has been presented to be a useful tool for radiation monitoring (1,2). Doubling of minisatellite mutation frequencies have been found in children after the Chernobyl accident (1,2). Minisatellite data on the second generation of the A-bomb survivors in Hiroshima and Nagasaki, did not show, however, any significant increase in germline mutations (3). One possible explanation could be different exposure conditions between Chernobyl and Hiroshima/Nagasaki, making these two minisatellite data imcomparable.

The purpose of our study is to investigate minisatellite mutation rates in peripheral blood lymphocyte DNA from children whose fathers have done a clean-up service at Chernobyl after the accident of nuclear power state in 1996. Altogether 232 Estonian families will be included into our study: there are 183 families (717 persons, 349 children) whose fathers have been at clean-up work in Chernobyl and 49 control families (147 persons, 49 children) whose fathers have not been in Chernobyl. From exposed families, approximately half of the children were conceived before the father was in Chernobyl. Thus our study group consists of 189 children and 160 intrafamily control children as well as 49 interfamily control children. A mean radiation dose among exposed fathers was 109 mGy. In our final analysis we will have at least 11 minisatellite markers, from which 5 minisatellites are being studied by PCR-based method and 6 minisatellites will be studied by Southern blot-based method.

We started a preliminary screening for 5 minisatellite alleles (APO B, MCT118, YNZ22, MCOB19 and HRAS). DNA has been extracted from blood lymphocytes and minisatellite sequences have been amplified by fluorescent PCR. DNA fragment sizes were studied with ABI automatic sequencer using a GeneScan fragment analysis software. So far, approximately 80% of all GeneScan analysis have been carried out. Our preliminary data on all subjects revealed 33 children whose minisatellite alleles are not consistent with their parents. With present minisatellite sequences, we have confirmed only 7 possible true positives so far. Four changes have turned out to be caused by false mothers and 22 by false fathers. Confirmation of the rest of the 10 found sequences are in process.

References:

1. Dubrova Y.E., Nesterov V.N., Krouchinsky N.G., Ostapenko V.A., Neumann R., Neil D.L. & Jeffrey A.J.. Human minisatellite mutation rate after the Chernobyl accident. *Nature 1996*; **380**:683-686

2. Dubrova Y.E., Nesterov V.N., Krouchinsky N.G., Ostapenko V.A., Vergnaud G., Giraudeau F., Buard J. & Jeffreys A.J.. Further evidence for elevated human minisatellite mutation rate in Belarus eight years after the Chernobyl accident. *Mutation Research 1997*; **381**: 267-278.

3. Neel J.V., Schull W.J., Awa A.A., Satoh C., Kato H., Otake M. & Yoshimoto Y. The children of parents exposed to atomic bombs: estimates of the genetic doubling dose of radiation for humans. *Am. J. of Human Genetics 1990*; **46**:1053-1072.