The following information pertains to questions 13-15

In 19995, Tiranti et al. (human Molecular Genetics 4:1421-1427) reported an instance of mitochondrial inheritance for hearing loss in a human pedigree. All siblings in a family of four (one male and three females) had hearing loss. The parents were deceased, so the parental phenotypes were unknown, although the parents were known to be first cousins. All four siblings were married to unrelated spouses, none of whom had hearing loss. The oldest sibling was female and had four children, all females and none with hearing loss. The second oldest was also female and had three children, two males and a female. Only the female child had hearing loss. The third sibling was male and had three children, two males and a female and none with hearing loss. The fourth sibling was female and had four children, three males and a female, all with hearing loss. (hint: to help yourself with your analysis, draw a pedigree of this family).

The researchers discovered a mutation in the DNA in one of the two mitochondrial serine tRNA genes. Below is a portion of the normal and mutant sequences of the tRNA gene:

Normal: GCTTTGGGGGGTTC

Mutant: GCTTTGGGGGGGTTC

Tirani et al. measured the proportion of mutant mitochondrial DNA in the somatic cells of members of this family with and without hearing loss. They found that the proportion of the mutant mitochondrial DNA in those individuals who had hearing loss ranged from 66 percent to 100 percent. Among those who did not have hearing loss, the proportion of mutant mitochondrial DNA ranged from 0 percent to 70 percent.

**13) Only one of the siblings (a female) had 100 percent mutant mitochondrial DNA. Based on the information above, which of the siblings had 100 percent mutant mitochondrial DNA?**

a) the first (oldest) sibling

b) the second sibling

c) one third sibling

d) the fourth (youngest) sibling

**14) Mutations in mitochondrial DNA are usually transmitted in a uniparental-maternal fashion in mammals. Why then do some of the remote siblings with hearing loss have children who do not have hearing loss?**

a) The females who had offspring without hearing loss were heteroplasmic.

b) There are two mitochondrial serine tRNA genes. The other tRNA gene sometimes compensates for the loss of function in the mutant tRNA gene.

c) Biparental inheritance of mitochondrial DNA caused some of the offspring to escape hearing loss.

d) None of the above

**15) Which of the following is the most probable cause of this mutation?**

a) slippage during DNA replication

b) tautomeric shift

c) None

d) SOS mutagenesis