

The famously eccentric biologist Pool Greenwater has dedicated his life to the study of gene expression in mammalian cells, using mice as a convenient model system. In his favorite mouse strain, sqk49, Pool has found that the growth factor GRW causes proliferation of liver cells. Pool has recently developed some mutant versions of his mice with the following genetic changes:

sqk49- Δ IRP mice have a mutation in the gene encoding the iron response protein that completely blocks transcription of the *IRP* gene.

sqk49-F Δ IRE mice have a deletion in the gene encoding ferritin that removes the IRE from the ferritin mRNA sequence.

sqk49-GRW Δ AT mice have a deletion that removes a ATTTAATTTAATTTAATTTAATTTA sequence from near the 3' end of the *GRW* gene.

1. What effects (if any) would you expect the mutation in the **sqk49- Δ IRP** mice to have on the production of ferritin protein? Explain your answer, being as specific as possible.

The IRP protein will be absent in cells of these mice. As a result, the IRE on the ferritin mRNA will never be bound by IRP. Thus, the ferritin mRNA will always be fully translated because the translation will never be blocked by IRP. The mouse's cells will produce high levels of ferritin protein, even when cellular [Fe] is low.

2. What effects (if any) would you expect the mutation in the **F Δ IRE** mice to have on the production of ferritin protein? Explain your answer, being as specific as possible.

The mutant ferritin mRNA will lack the IRE, so it could never be blocked by IRP, even at low iron concentrations. The concentration of ferritin protein would always be high.

3. Pool has noticed that he has trouble keeping his **sqk49-GRW Δ AT** mice, as most of them die from liver cancer. Can you provide him a logical explanation for this observation? Please be as specific as possible.

It would appear that a sequence encoding an AU-rich element has been deleted from the gene. The *GRW* mRNA is normally made unstable by this element. The mutant version of *GRW* mRNA is too stable, and results in the production of too much GRW protein. This causes excessive liver cell proliferation (cancer).