A fast selenium derivatization strategy for crystallization and phasing of nucleic acid structures

The growing number of biologically important nucleic acid sequences (DNA and RNA) demands a fast and reliable method for their *de novo* three-dimensional structure determination. In this work, we described a fast and inexpensive strategy for the crystallization and phasing of structures of nucleic acid and nucleic acid/protein complexes.

In the early 1990's, covalent modification of nucleic acid using Selenium was introduced as a new approach to facilitate crystal structure determination of nucleic acid (in case of failure of classical molecular replacement or heavy atoms derivatives techniques, such modification allows to use the powerful multiwavelength anomalous dispersion technique to tackle the phase problem). Hovewer, due to a cumbersome and expensive synthesis of such Seleno-labeled nucleic acid, only few structures have been determined and halogen-modification was till now favored (Bromo- or Iodo-modification, although extremely sensitive to radiation damage, see Fig. 1).

We have developed an efficient strategy for crystallization and structure determination of nucleic acids by exploiting the similar crystallization properties of 2'-$SeCH_3$- and 2'-OCH_3-modification. Indeed, the incorporation of 2'-OCH_3 into nucleic acids is less expensive, easier and allows large crystal screening to be done. Once a crystal is obtained with the 2'-OCH_3-modified sequence, 2'-OCH_3 is then replaced by the 2'-$SeCH_3$ counterpart, providing an inexpensive and fast approach to the three-dimensional structure determination of various nucleic acid and nucleic acid/protein complexes.
In addition, our data show that 2'-$SeCH_3$-modification has an increased resistance to X-ray radiolysis in comparison with commonly used halogen-modification (Fig. 1), which permits collection of experimental electron density maps of remarkable quality (Fig. 2).

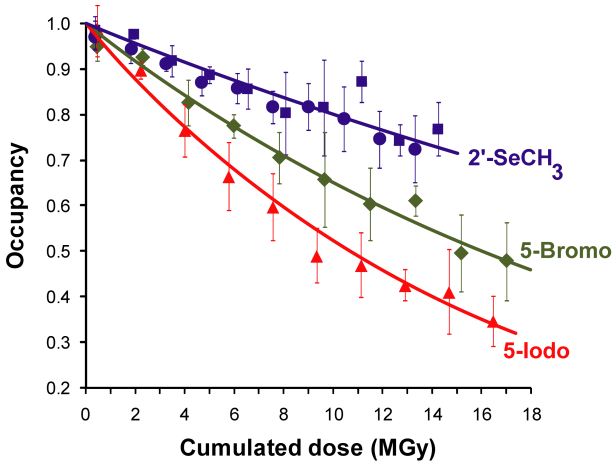

Figure 1: *Site-specific radiation damage studies of modified RNA. The plot clearly shows a greater resistance of 2'-$SeCH_3$ towards radiolysis over classical Bromo- and Iodo-modified RNA.*

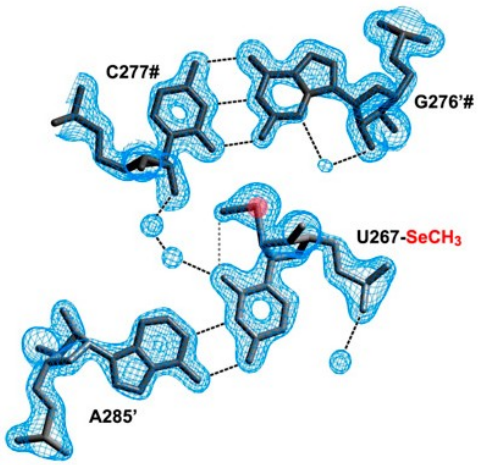

Figure 2: *Experimental electron density map obtained with 2'-$SeCH_3$-modified RNA.*

Publications

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