

Antisense targeting in cell culture with radiolabeled DNAs —a brief review of recent progress—

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The promise of antisense targeting that any tissue with a unique genetic expression can be specifically localized with radioactivity in the living subject is the holy grail that drives this research today. If antisense targeting were to achieve even a fraction of its promise, the results could well lead a revolution in diagnostic nuclear medicine. Despite its obvious complexities, antisense targeting with radiolabeled oligomers such as DNA is making considerable progress in cell culture. As is documented in this brief review, evidence is becoming overwhelming that an antisense mechanism is probably responsible for the accumulation in tumor cells in culture of radiolabeled DNAs with base sequences antisense to target messenger RNAs (mRNAs). That an increased accumulations of these DNAs compared to control DNAs has now been seen in a substantial number of tumor cell types and mRNA targets largely eliminates any possibility of an aptameric effect being responsible for these specific accumulations. In addition, the number of antisense DNAs accumulating specifically in cells in culture has been shown to be orders of magnitude larger than that expected on the basis of steady state mRNA levels. Thus, two of the main concerns regarding antisense targeted, namely that the mechanism of localization may not be attributed to antisense and that the degree of accumulation will be impractically low for imaging, have been addressed in recent research. The remaining obstacle to successful targeting may be delivery. This review will provide a brief review of recent results, primarily from the laboratory of one of the authors (DJH), obtained in tissue culture in studies of antisense targeting and will conclude with several suggestions for future approaches.

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