In this issue, Da Costa and coworkers (page 5039) explore the subcellular localization of the RPS19 protein and the effects of mutations on this localization. RPS19 was detected in the nucleoli of transfected mammalian cells. Structure-function analysis revealed two nucleolar localization signals (NoSs) in RPS19. Interestingly, 2 DBA patient–derived mutations, each of which localized to 1 of the 2 NoSs, resulted in a failure of targeting RPS19 to the nucleolus.

This study provides the first link between DBA patient–derived mutations in *RPS19* and mislocalization and misexpression of the RPS19 protein. The study also adds to the growing list of protein-targeting signals that direct subnuclear architecture. Perhaps most important, the paper helps to frame the future of research in the DBA field. It now becomes important to determine whether misexpression of *RPS19* affects ribosome assembly, erythroblast maturation, or even the steroid responsiveness of DBA bone marrow cells.

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## Additional alpha applications

Modern radioimmunotherapy, the use of monoclonal antibodies to deliver radioisotopes to tumor cells, has been under development for 2 decades. Nearly all of this work has focused on the use of agents that carry beta particle–emitting isotopes. Beta particles have relatively low energy and long ranges, which make them most useful for radiosensitive tumors of considerable size, such as lymphomas. These investigations led to the first approval of a radioimmunopharmaceutical last year, known as ibritumomab tiuxetan, for B-cell non-Hodgkin lymphomas. But the emission characteristics of beta particles make it difficult for such agents to kill individual cancer cells or nonsensitive tumor types. As an alternative, alpha-particle emitters and alpha-particle generators are capable of extraordinarily potent single-cell kill of a wide variety of tumor types. Trials of alpha-particle emitters in the United States and Europe are now focusing on leukemias and lymphomas.

In this issue, Bethge and colleagues (page 5068) have now reported a new use for alpha-particle radioimmunotherapy: the selective reduction of host T cells in the setting of allogeneic bone marrow transplantation. This novel approach matches the unique characteristics of the alpha particle mechanism to an important problem still facing bone marrow transplantation. These investigators used a canine transplantation model in which an antibody to the T-cell receptor labeled with the short-lived alpha-emitting radiometal bismuth 213 is substituted for more traditional total body irradiation to suppress immune responses. The therapy was characterized by safety and prompt engraftment. Such an approach should be translatable into human applications and might avoid the traditional toxicities associated with irradiating the entire body simply to reduce a select population of T cells. This strategy could be incorporated into "nonmyeloablative" transplantation procedures because of its selectivity and lack of toxicity.

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