BLOOD CANCER DISCOVERY

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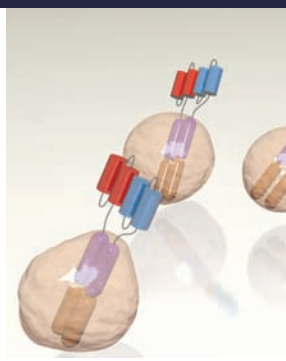

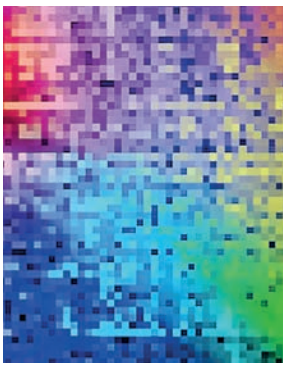

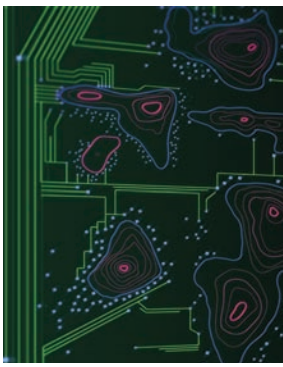

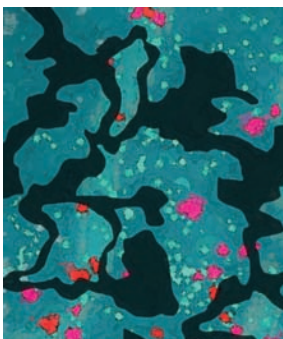

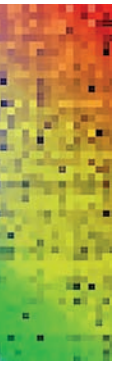

ON THE COVER Multiple myeloma often relapses following CAR T cell therapy. The relapsing myeloma cells often lose or decrease the expression of the CAR-targeted antigen, suggesting antigen escape prevention may increase durability of the remission. In this issue, Eric Smith, Renier Brentjens and colleagues present approaches for simultaneously targeting BCMA and GPRC5D myeloma antigens by a single CART infusion. BCMA/GPRC5D dual-specific CAR T cells eliminate myeloma cells positive for both antigens, and protect mice from rechallenge with BCMA-negative myeloma. Among three orthogonal approaches, the best CAR T performance is achieved when BCMA and GPRC5D CARs are encoded by a bicistronic vector. The results pave the way to testing whether the dual-antigen CAR therapy would prevent antigen escape and extend the remission in patients with BCMA+ GPRC5D+ myeloma in clinical trials. For details, please see the article by Fernández de Larrea *et al.* on page 146 and the accompanying commentary by Simon and Riddell on page 130.

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