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RGB marking facilitates multicolor clonal cell tracking

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Abstract: We simultaneously transduced cells with three lentiviral gene ontology (LeGO) vectors encoding red, green or blue fluorescent proteins. Individual cells were thereby marked by different combinations of inserted vectors, resulting in the generation of numerous mixed colors, a principle we named red-green-blue (RGB) marking. We show that lentiviral vector–mediated RGB marking remained stable after cell division, thus facilitating the analysis of clonal cell fates in vitro and in vivo. Particularly, we provide evidence that RGB marking allows assessment of clonality after regeneration of injured livers by transplanted primary hepatocytes. We also used RGB vectors to mark hematopoietic stem/ progenitor cells that generated colored spleen colonies. Finally, based on limiting-dilution and serial transplantation assays with tumor cells, we found that clonal tumor cells retained their specific color-code over extensive periods of time. We conclude that RGB marking represents a useful tool for cell clonality studies in tissue regeneration and pathology.

Statement: Our work establishes a completely new way of fast and easy clonal cell tracking based on individual color coding. The novel technique might be of great interest for many research groups working in the fields of regenerative medicine, transplantation, stem cell biology or tumor biology. The work represents the result of interdisciplinary efforts by three research groups of the SFB841 "Liver inflammation" in cooperation with a group from the Heinrich-Pette-Institute.

This work was performed at the Clinic for Stem Cell Transplantation in the Research Department Cell and Gene Therapy headed by Boris Fehse. The group has strong research interests in the fields of gene therapy and retroviral gene transfer. The first author, biochemist Kristoffer Weber is a former PhD student and now postdoc in this group. The close collaboration with the groups of Maura Dandri, Daniel Benten, Jörg Pollok (all UKE) and Carol Stocking (HPI) enabled the successful development of the new technology. The work was supported by the SFB841 and the Integrated Graduate School "Inflammation and Regeneration".