Nature Methods: CNIC presents iFlpMosaics, an innovative genetic toolkit for the study of gene function

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iFlpMosaics is a new technology presented in Nature Methods that allows the modification and study of gene function in mouse models, advancing research on diseases caused by somatic mutations, such as cancer and vascular malformations.

A team at the Centro Nacional de Investigaciones Cardiovasculares (CNIC), led by Dr. Rui Benedito, has developed a comprehensive set of innovative genetic tools and mouse lines, called iFlpMosaics, designed to enhance the study of gene function and its implications in health and disease.

The groundbreaking study, published in Nature Methods, presents a pioneering approach that overcomes critical limitations of existing methods for generating genetic mosaics. These innovations will enable scientists to more accurately investigate the effects of somatic mutations on cellular biology and disease.

The study highlights the **iFlpMosaics** toolkit's utility across different experimental setups, detailing how it allows scientists to track the effects of single or multiple gene deletions within the same tissue. This advance opens the way to deeper insight into the function of genes in cell biology, regeneration, and disease.

Understanding gene function is pivotal for the progress of biomedical research. Traditional biomedical genetic studies compare cells from distinct mutant and control animals, a method that often fails to account for the differing epigenetic landscapes and tissue microenvironments within each animal. “This disparity can lead to confusing results, complicating the interpretation of gene function,” explained Dr. **Benedito**.

The iFlpMosaics toolkit is unburdened by these shortcomings and allows researchers to induce genetic mosaics with high throughput and precision, making it easier to study cell-autonomous gene function directly within the same organism.

"Our work with these new genetic tools highlights the importance of generating genetic mosaics from identical progenitor cells, within the same animal, if we want to fully understand the function of different genes in multiple cell types during organ development or in disease models" said **Dr. Irene García González**, the first author on the study.

Current technologies for inducing genetic mosaics, such as MADM (Mosaic Analysis with Double Markers) or Cre-dependent mosaics, are hampered by technical issues related to low efficiency or reliability. The iFlpMosaics toolkit overcomes these issues, offering a robust platform for the ratiometric induction and clonal tracking of fluorescently labeled wildtype and mutant cells.

The toolkit not only enhances the understanding of genetic mutations in tissue development and disease processes, but also facilitates the study of complex interactions between cells within their microenvironment.

"iFlpMosaics offers a big step forward for researchers studying diseases caused by somatic mutations, such as cancer and vascular malformations” said Dr. Rui Benedito. “It’s precision and versatility provide an important resource for anyone seeking a better understanding of gene function in normal organ development and function, as well as in disease settings.”

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- *Garcia-Gonzalez, I., Gambera, S., Rocha, S. F., Regano, A., Garcia-Ortega, L., Lytvyn, M., Diago-Domingo, L., Sanchez-Muñoz, M. S., Garcia-Cabero, A., Zagorac, I., Luo, W., De Andrés-Laguillo, M., Fernández-Chacón, M., Casquero-Garcia, V., Lunella, F. F., Torroja, C., Sánchez-Cabo, F., & Benedito, R. (2024). iFlpMosaics enable the multispectral barcoding and high-*

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