Graphene liquid-enclosure facilitates single protein analysis in whole cells by electron microscopy.

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Membrane proteins regulate many important cellular functions via dynamic assembly into active complexes. Yet, analytical methods to study their distribution in the intact plasma membrane are still limited. Therefore, we used a graphene liquid-enclosure to enable high resolution electron microscopy (EM) of single, whole cells for the analysis of membrane protein distribution in the context of the corresponding cellular region.
For this purpose, SKBR3 cells were grown on silicon microchips and stained with quantum dots (QDs) bound to specific peptides to label the ErbB2 growth factor receptor. The samples were covered with graphene films and imaged with correlative light microscopy and EM. Scanning transmission EM (STEM, 200 kV) enabled statistical analyses of the distribution into single, paired and clustered ErbB2 proteins. We compared different membrane structures, such as ruffles or tunneling nanotubes, to flat cellular regions and found increased homodimerization of ErbB2 proteins at these sites.
In conclusion, the graphene liquid-enclosure allowed single-molecule analysis of membrane proteins in intact, hydrated cells.

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