

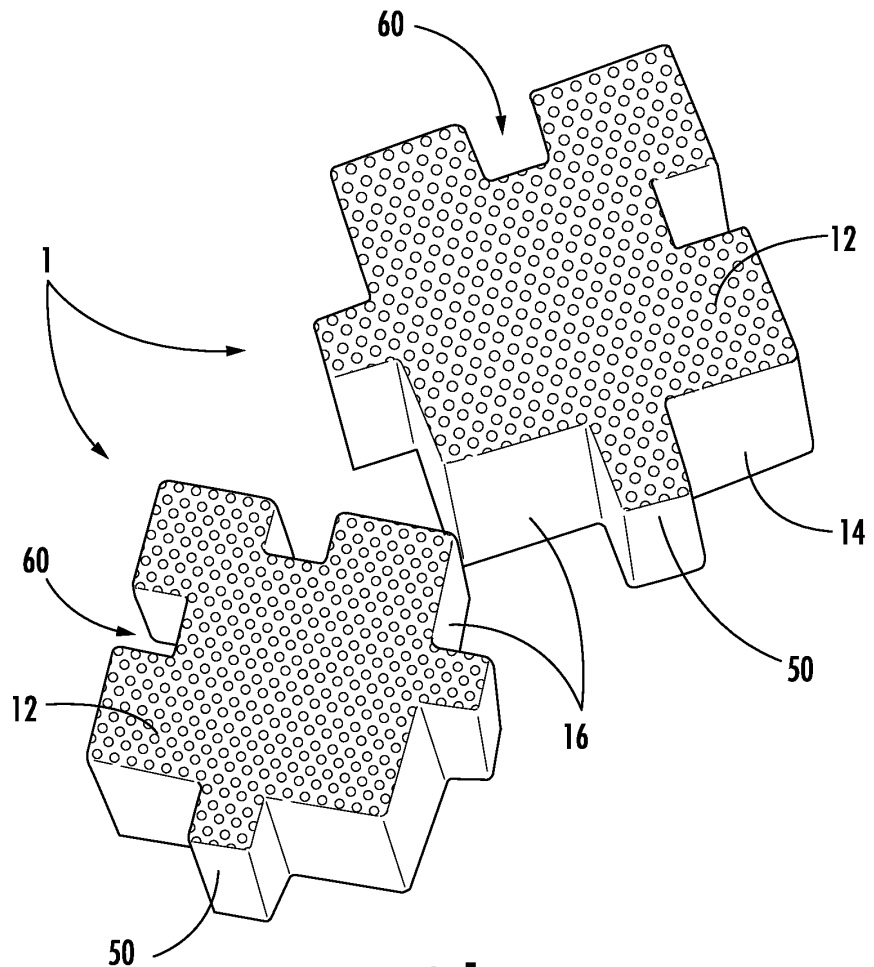


FIG. 1

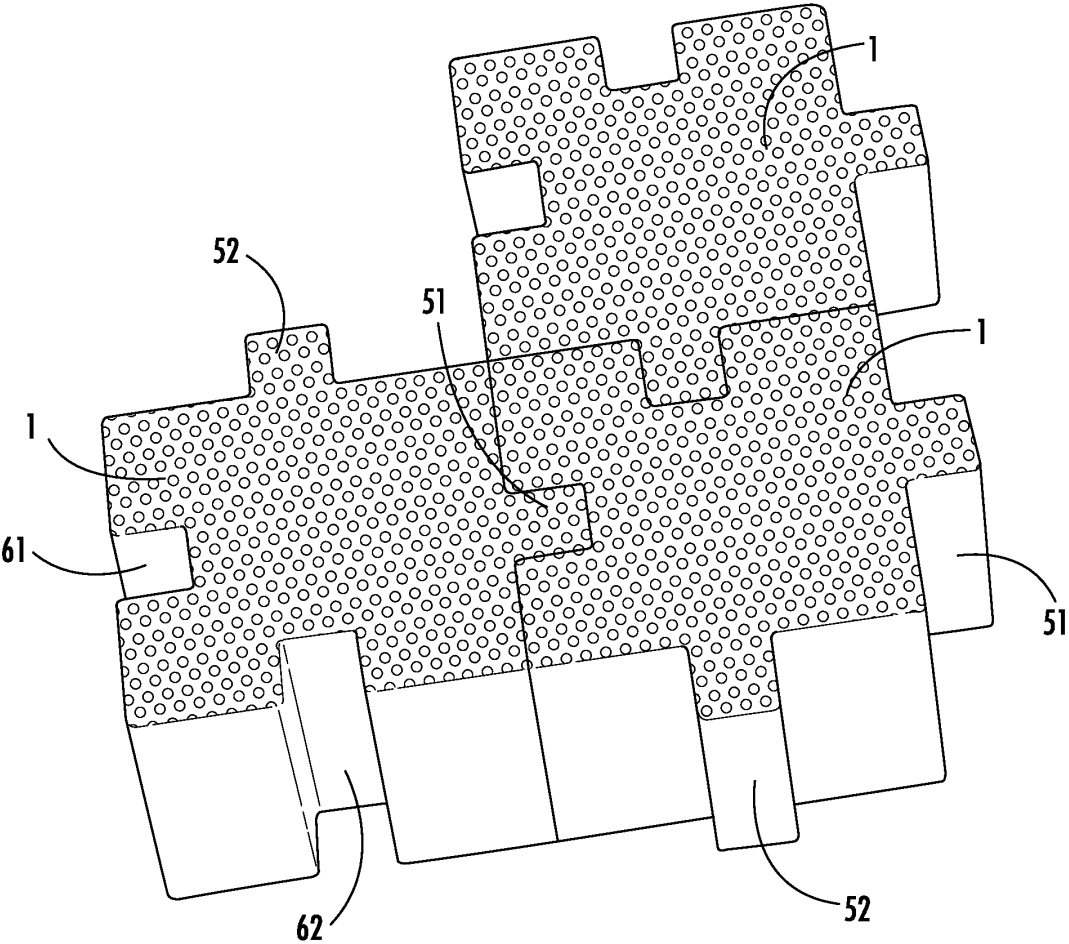
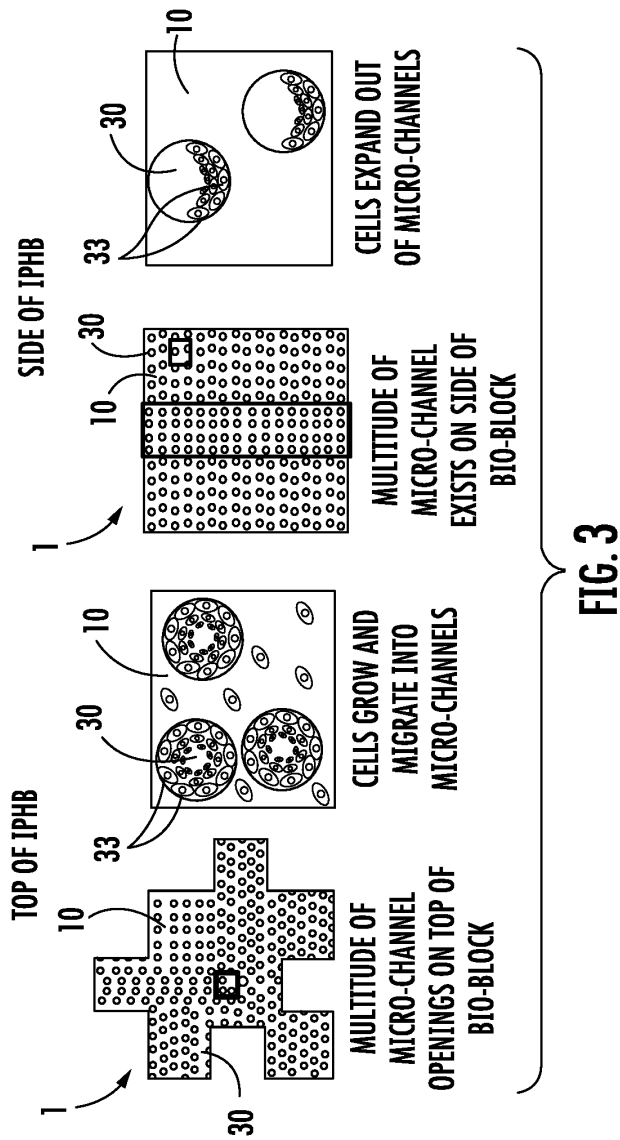


FIG. 2



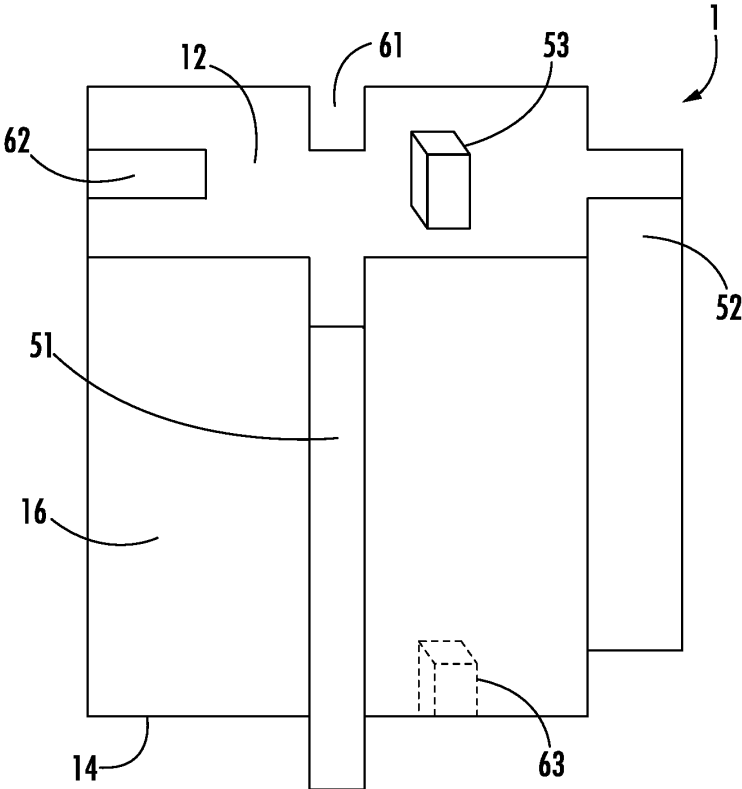


FIG. 4

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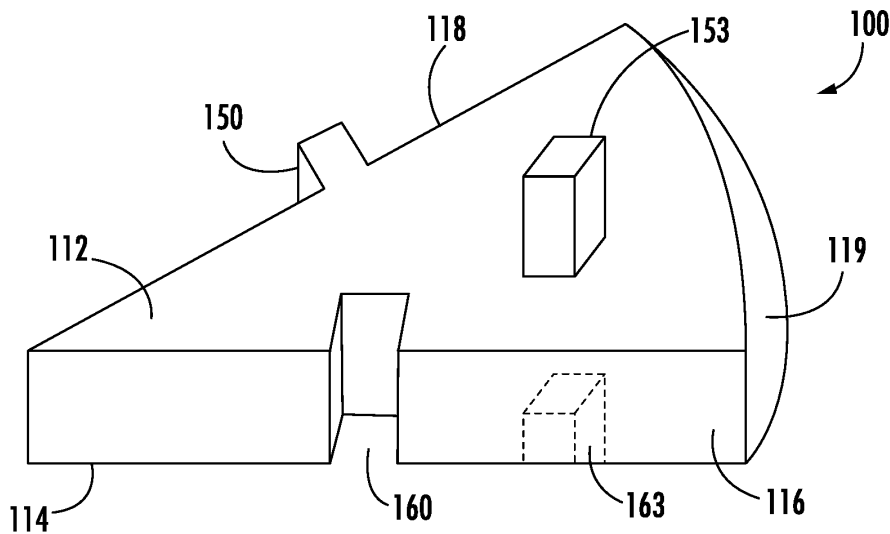


FIG. 5

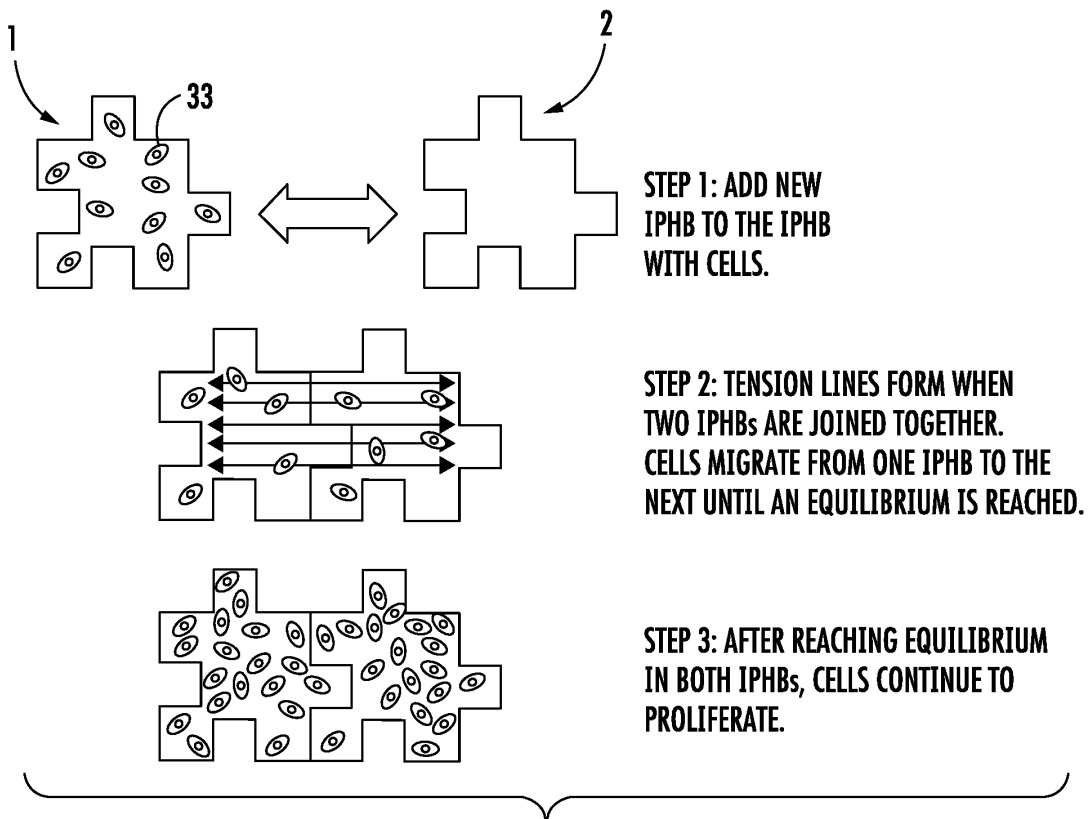
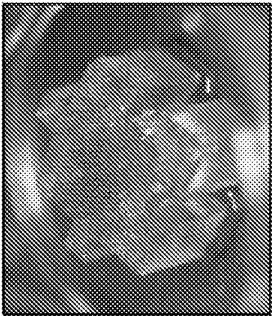
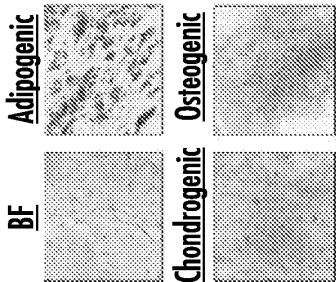
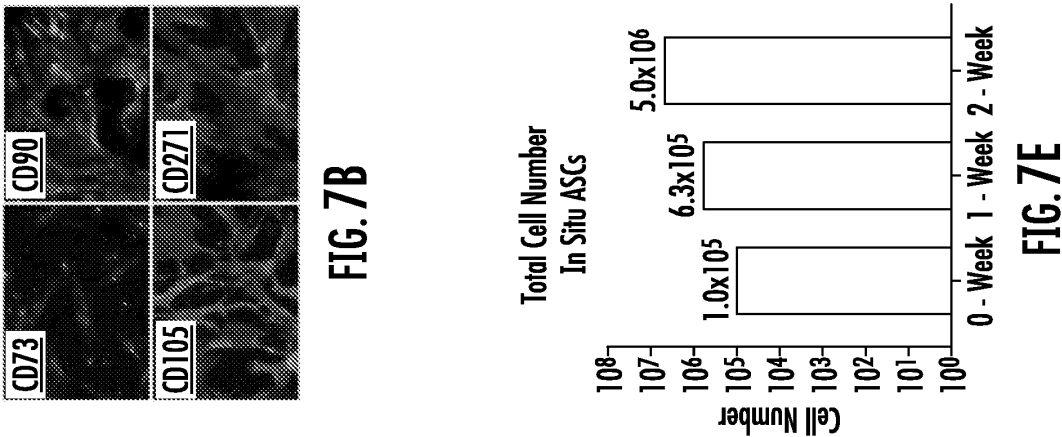
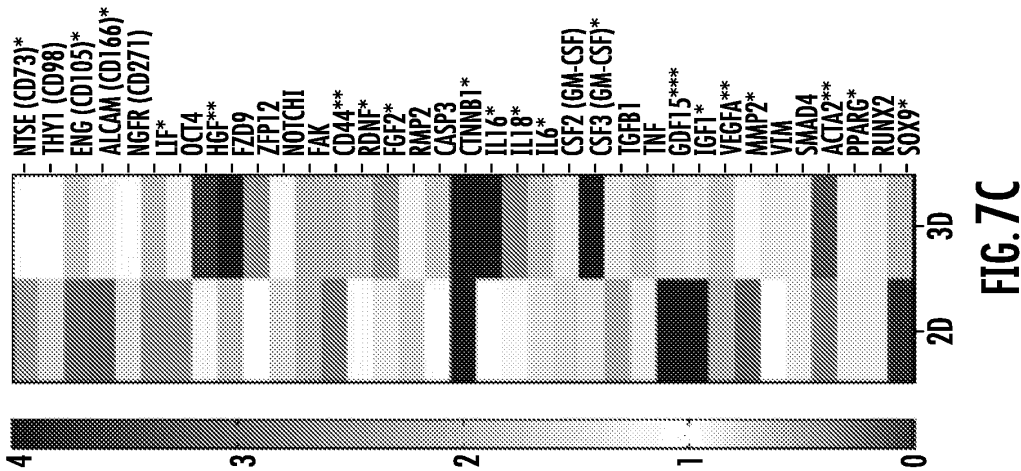
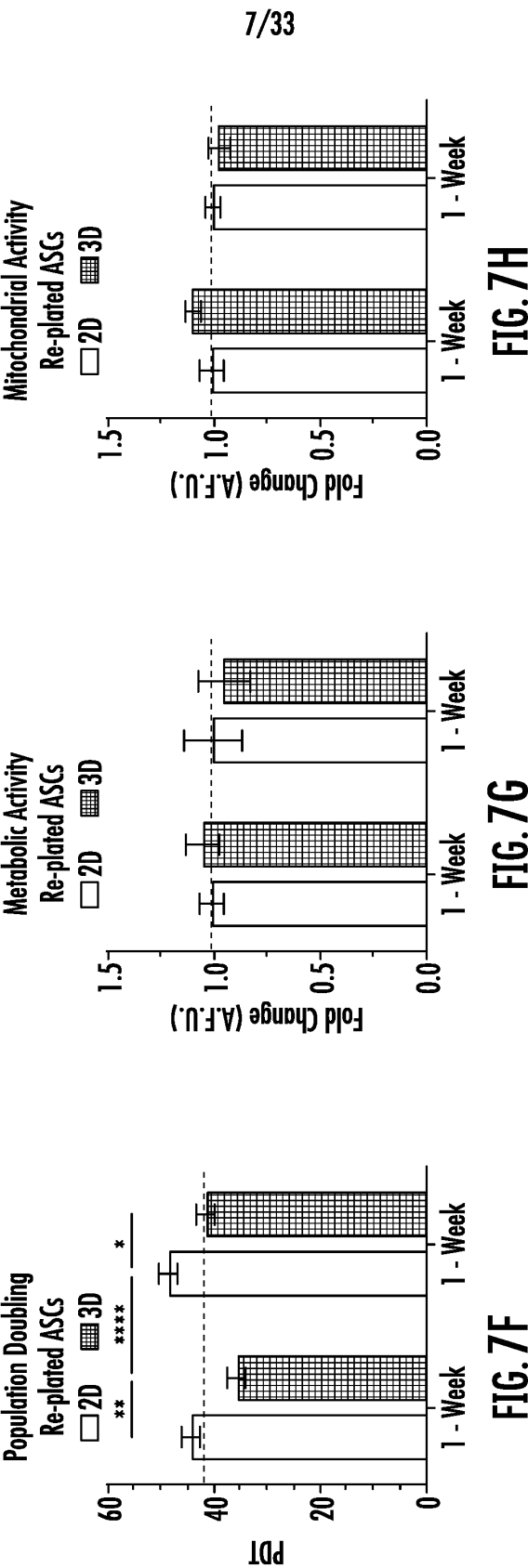


FIG. 6





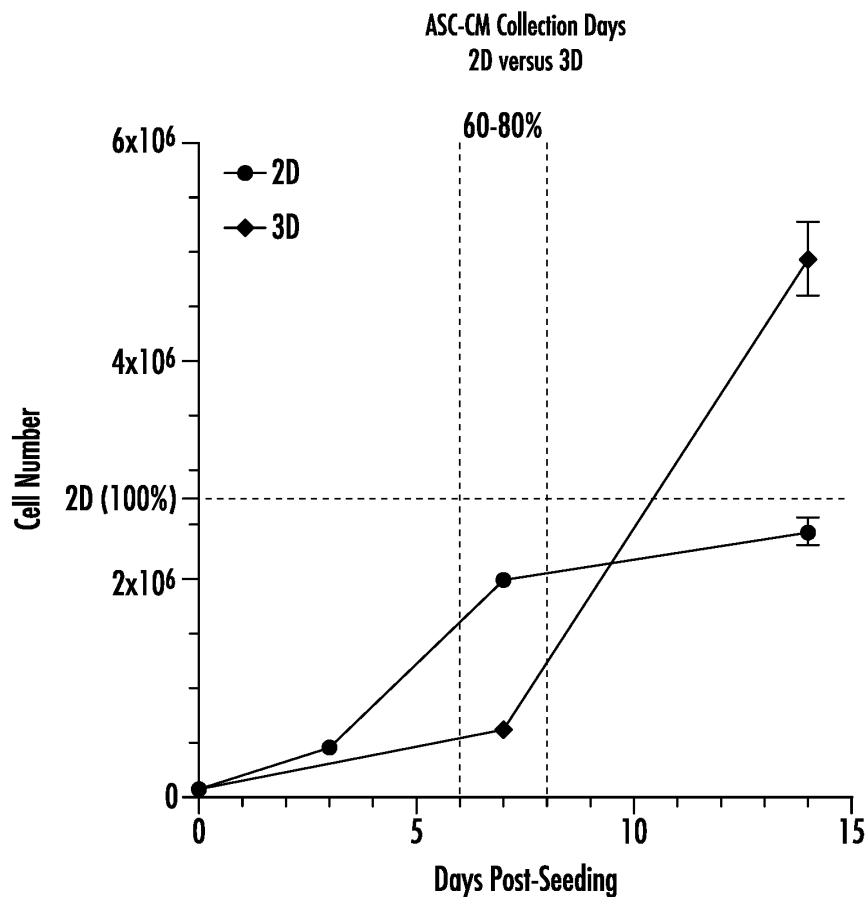


FIG. 8

ASC Growth Curve for 2D and 3D to Establish ASC-CM Collection Days. ASCs cultured in the 3D system had a slight delay in reaching the growth phase likely due to an initial migratory phase to equally distribute throughout hydrogel microarchitecture, but quickly overcame the relative cell number in 2D and eventually exhibited a higher rate of proliferation in 3D. Therefore, cell numbers were assessed in advance for 2D and 3D to determine the optimal days for collection on ASC-CM to standardize relative media-per-cell ratios. Based on prior literature, collection of ASC-CM in 2D at 60-80% confluency was desired and days 6-8 were selected to collect ASC-CM. Media volumes were adjusted accordingly to account for differences in cell numbers between 2D and 3D.

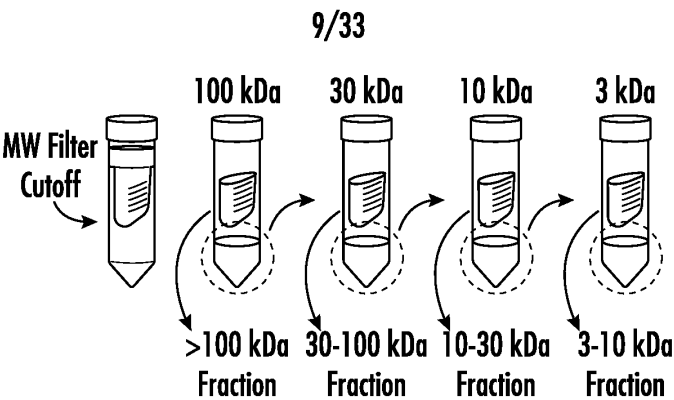


FIG. 9A

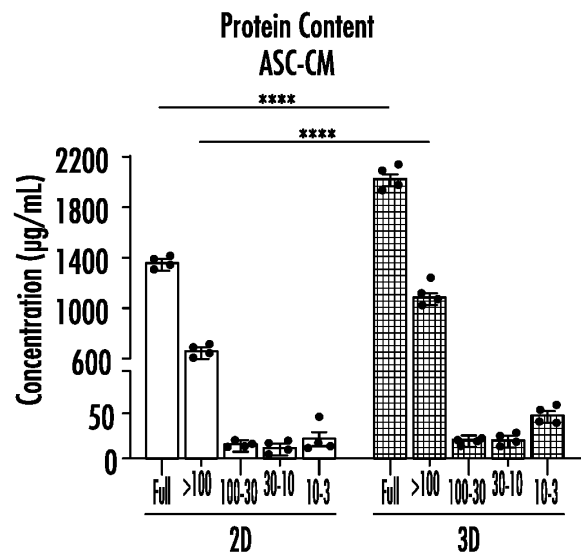


FIG. 9B

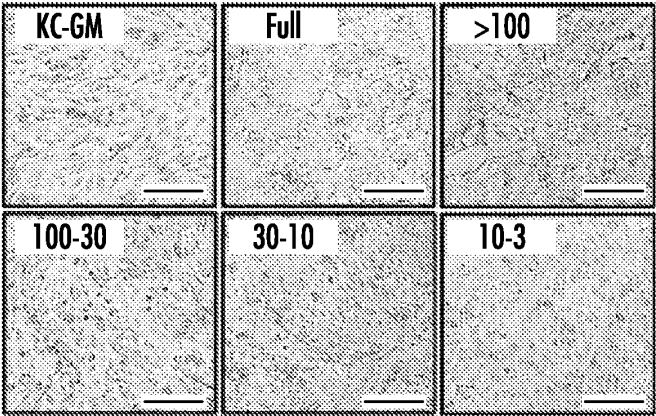


FIG. 9C

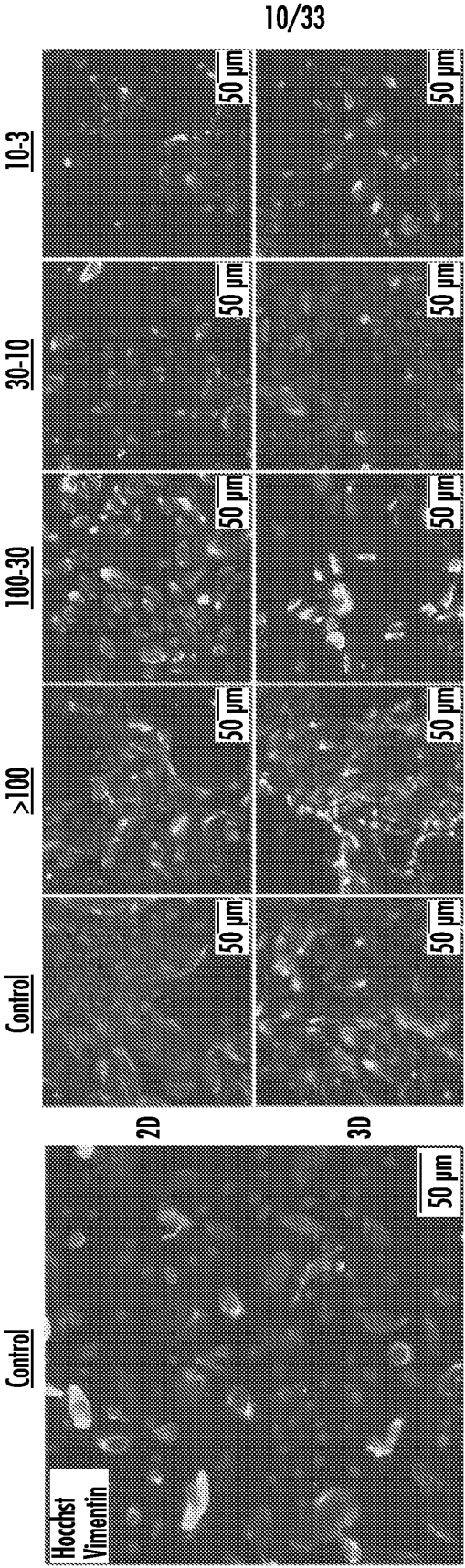


FIG. 9D

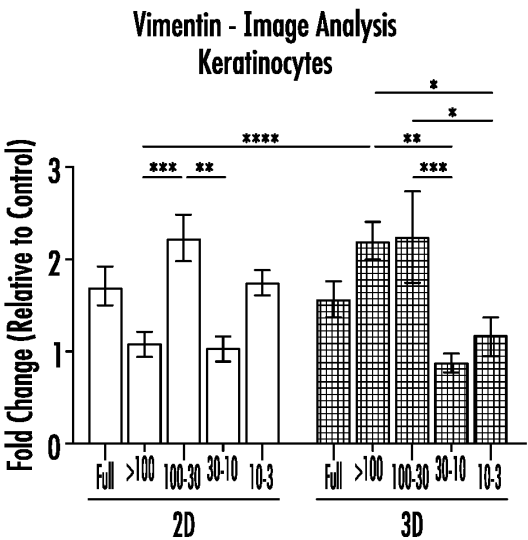


FIG. 9E

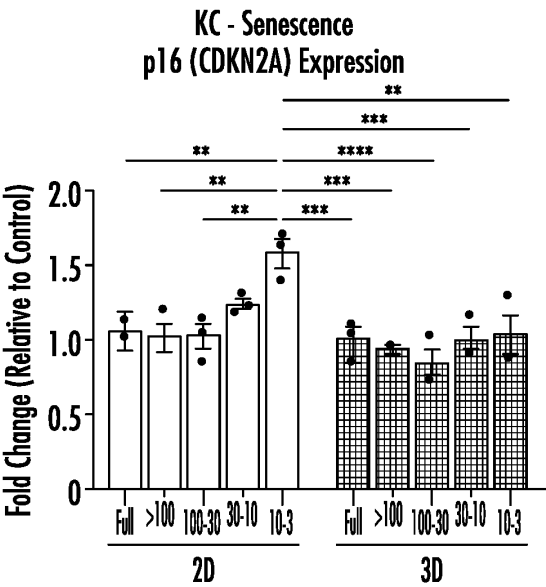


FIG. 9F

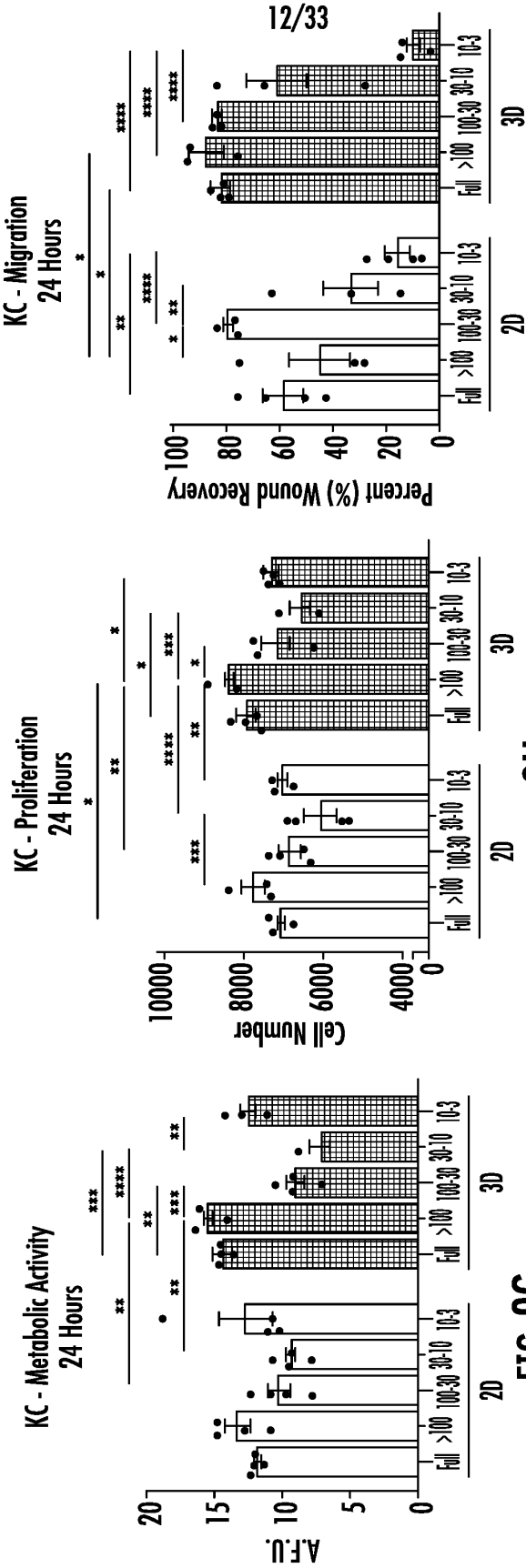


FIG. 9I

FIG. 9H

FIG. 9G

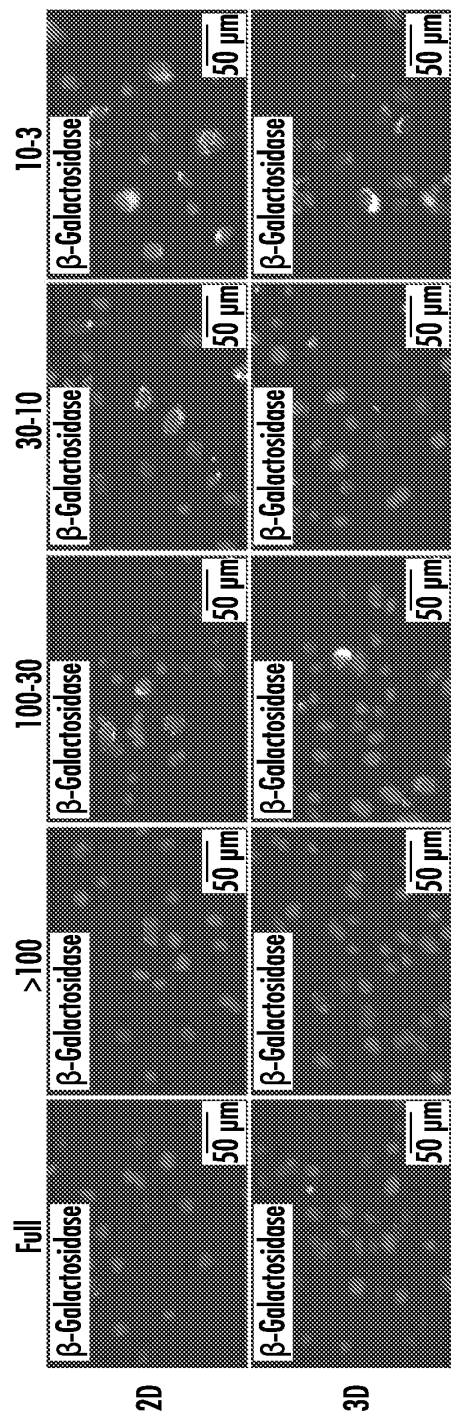


FIG. 10

Image analysis of KC Senescence after MW Stratified ASC-CM Treatment: Representative images of KCs after treatment with KC-GM supplemented with difference ASC-CM MW concentrates for 24 hours. B-Galactosidase activity was used as a surrogate measure for senescence. Lower MW fractions of ASC-CM appeared to induce senescence in KC populations. This corroborated the qRT-PCR data for p16 previously discussed.

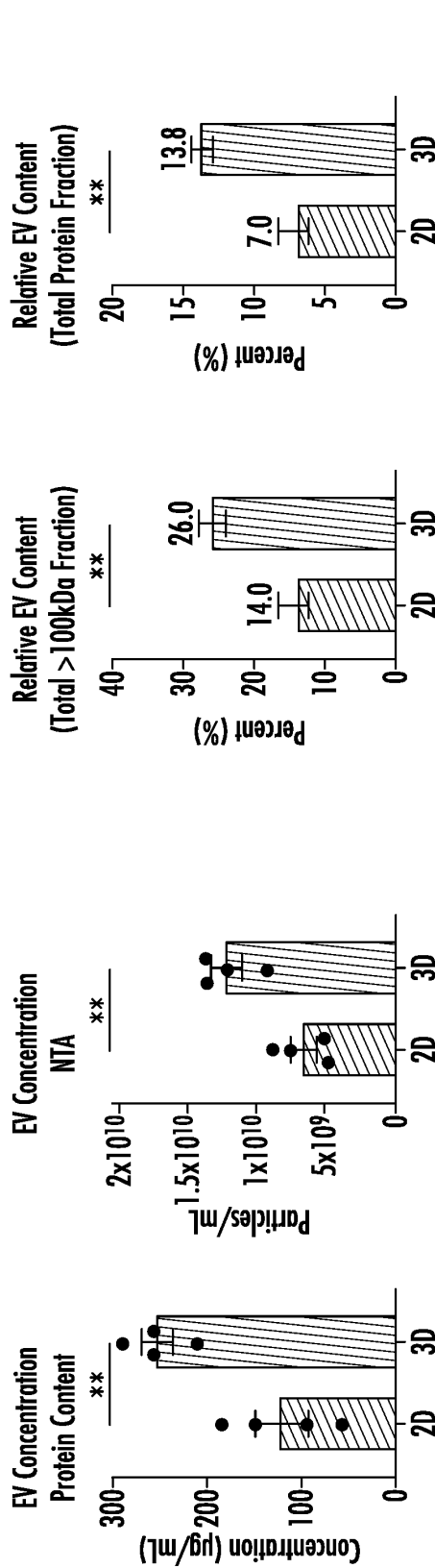


FIG. 11A

FIG. 11B

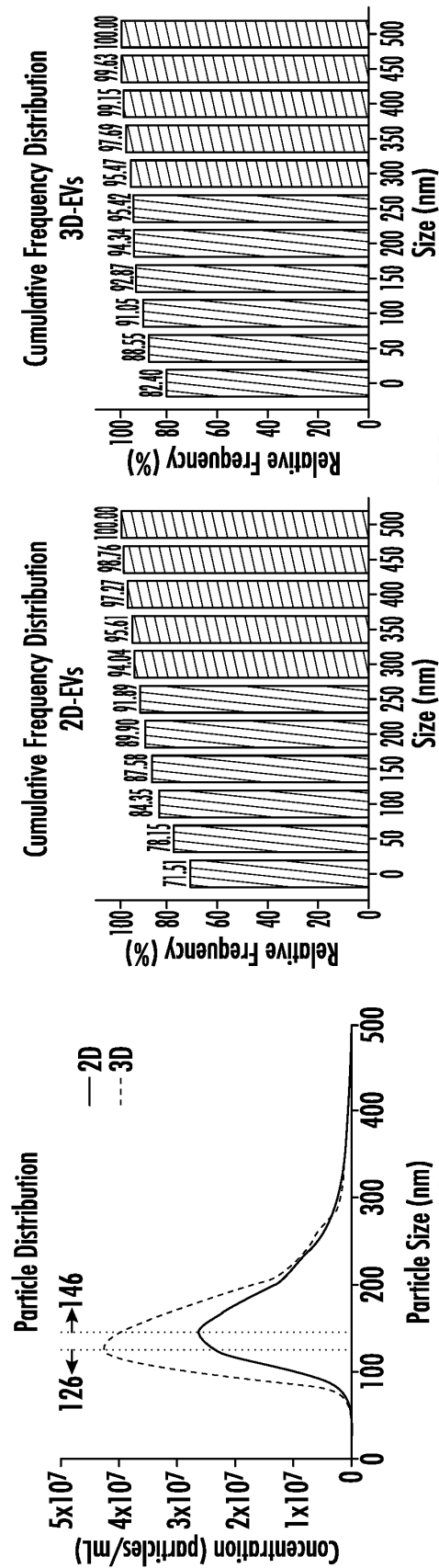


FIG. 11C

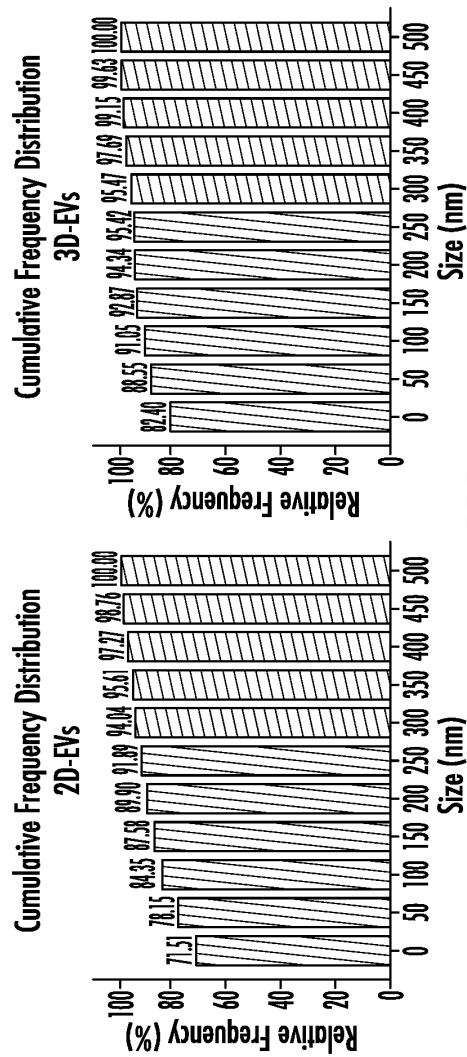
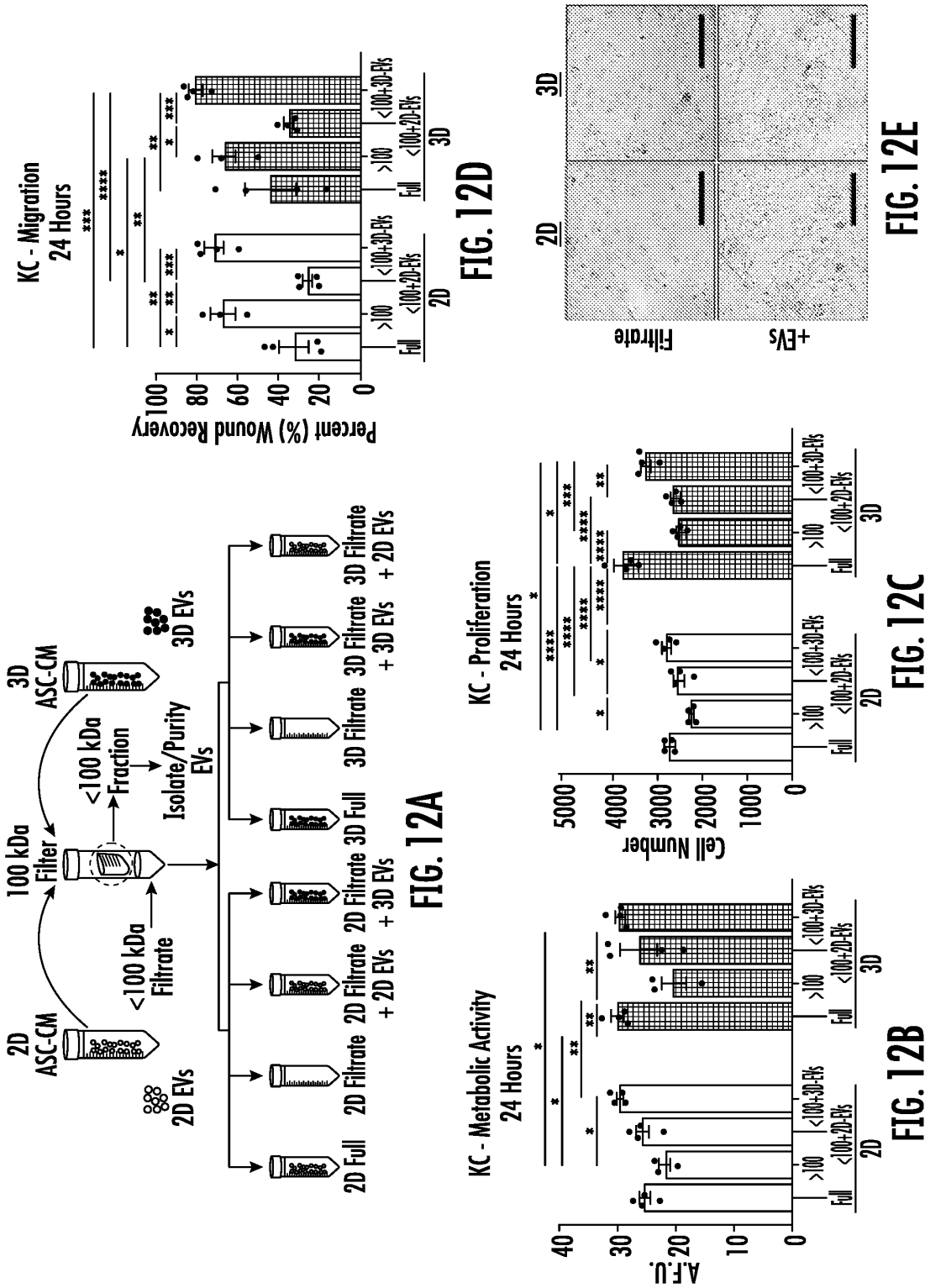


FIG. 11D



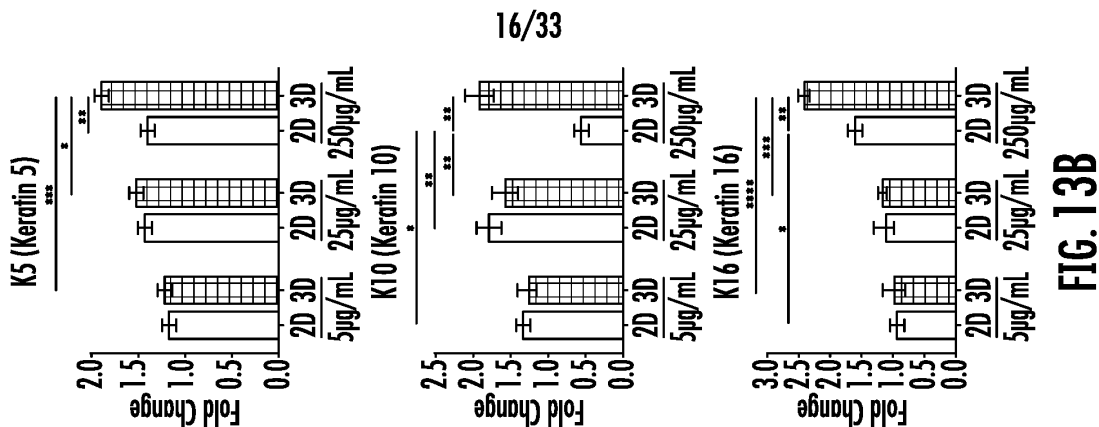


FIG. 13B

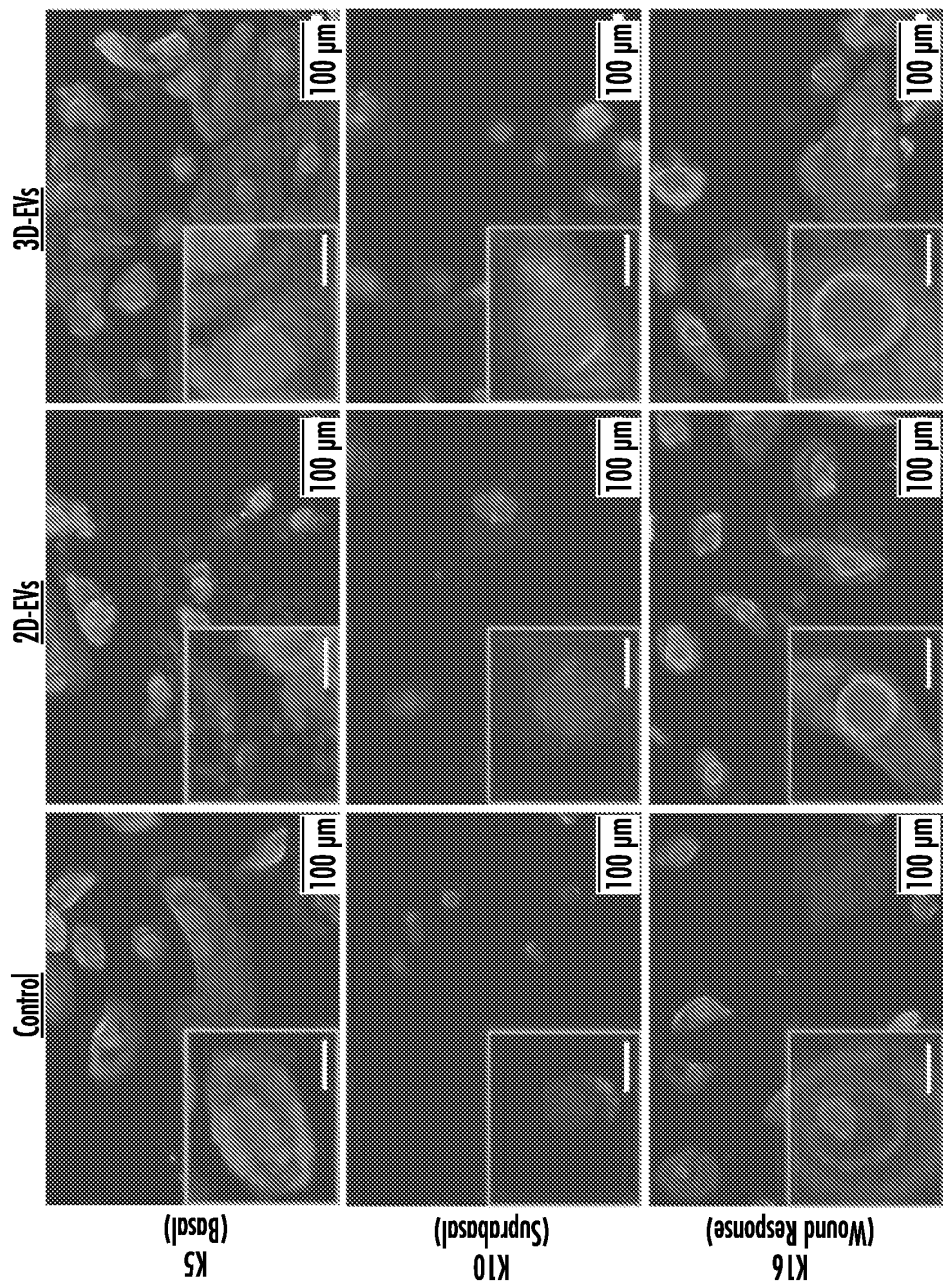


FIG. 13A

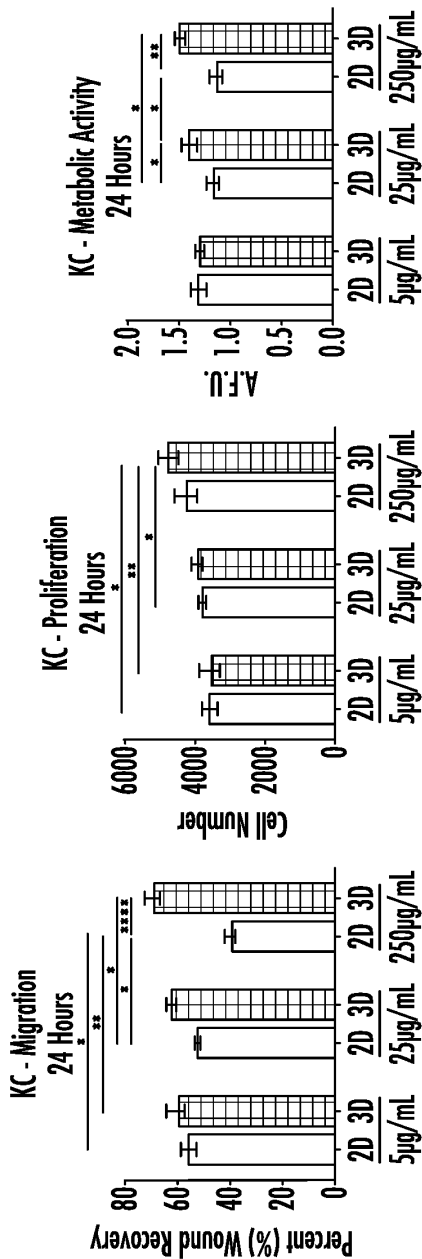


FIG. 14A

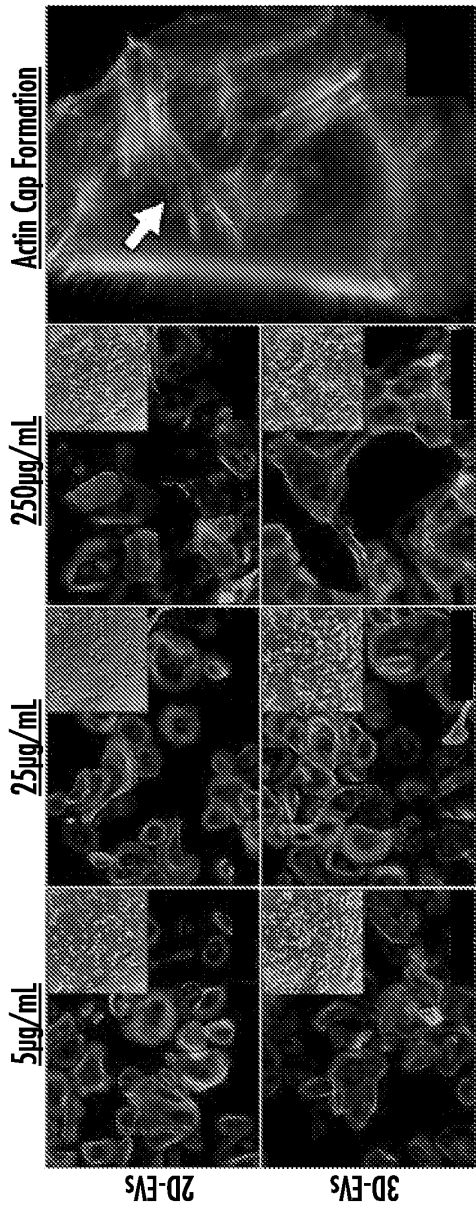


FIG. 14B

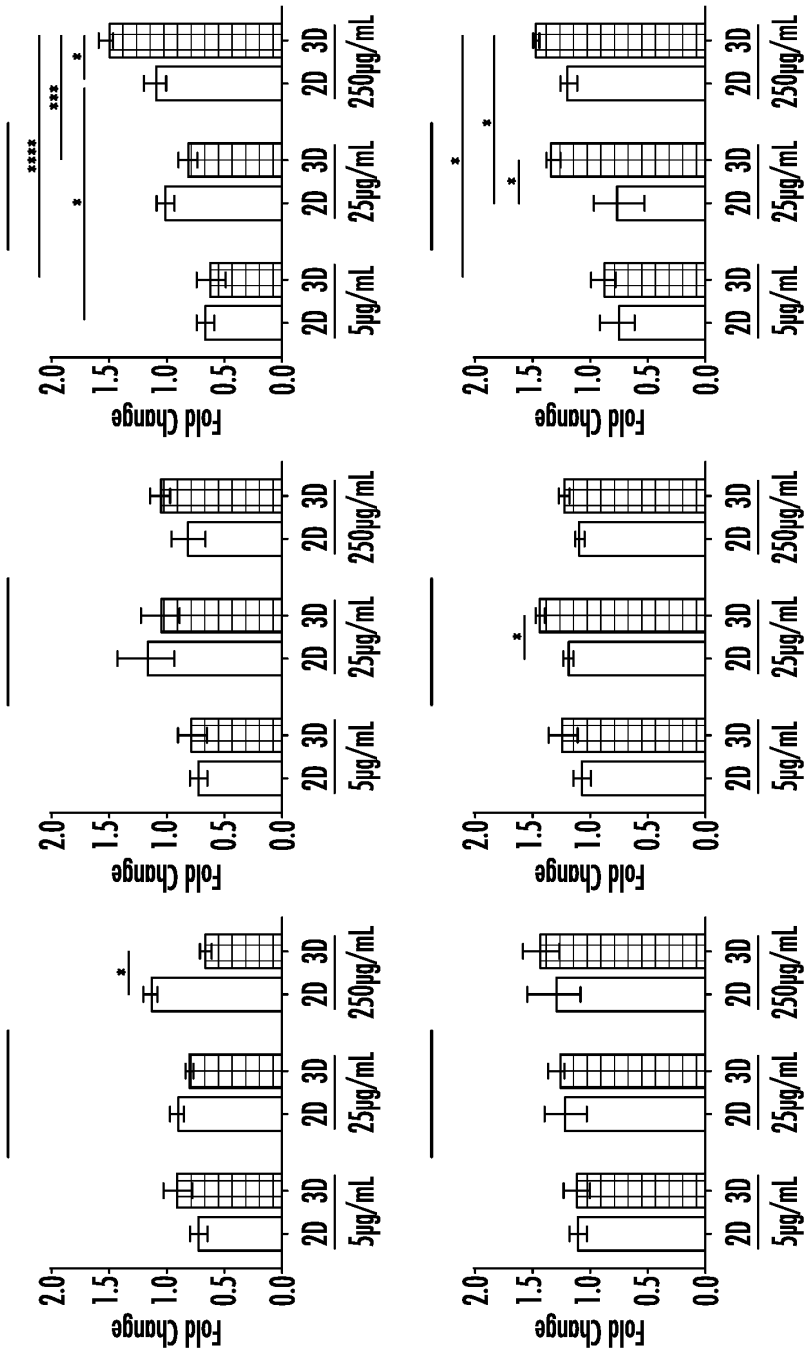


FIG. 14C

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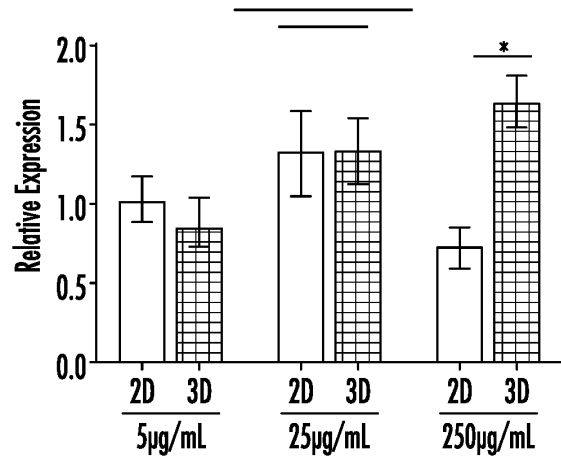
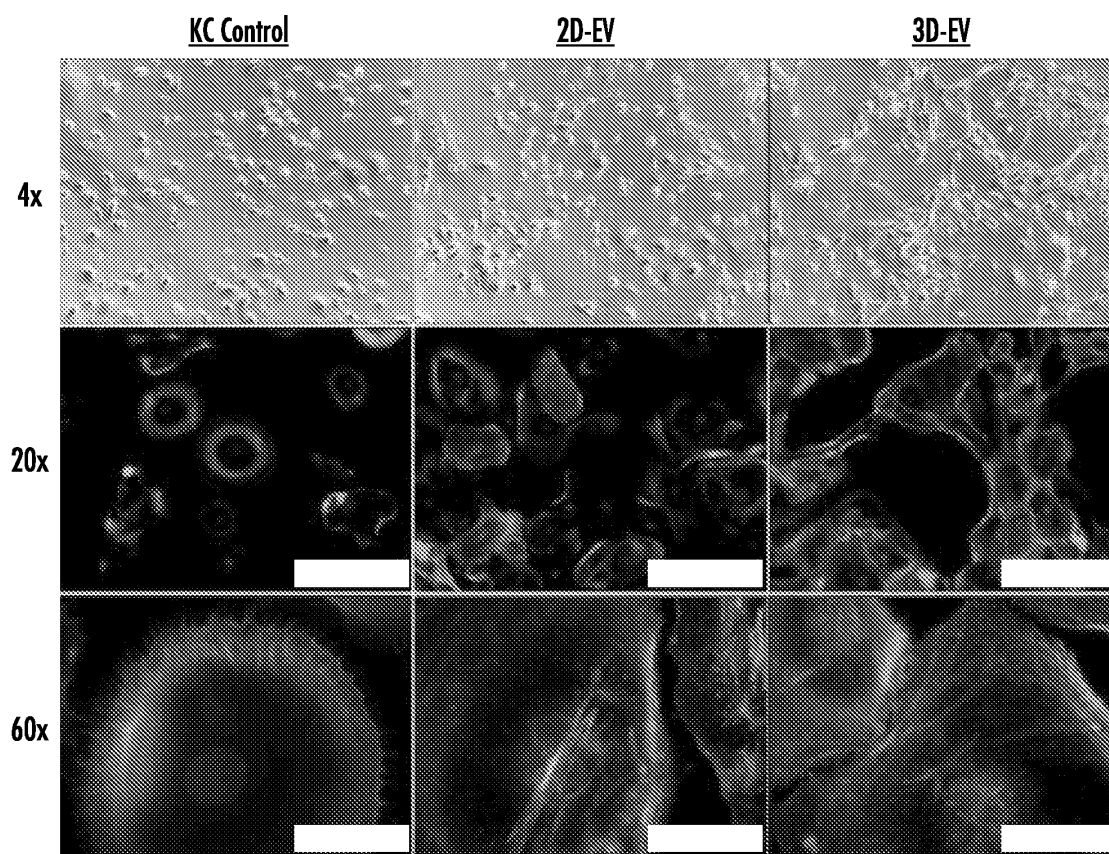


FIG. 14D

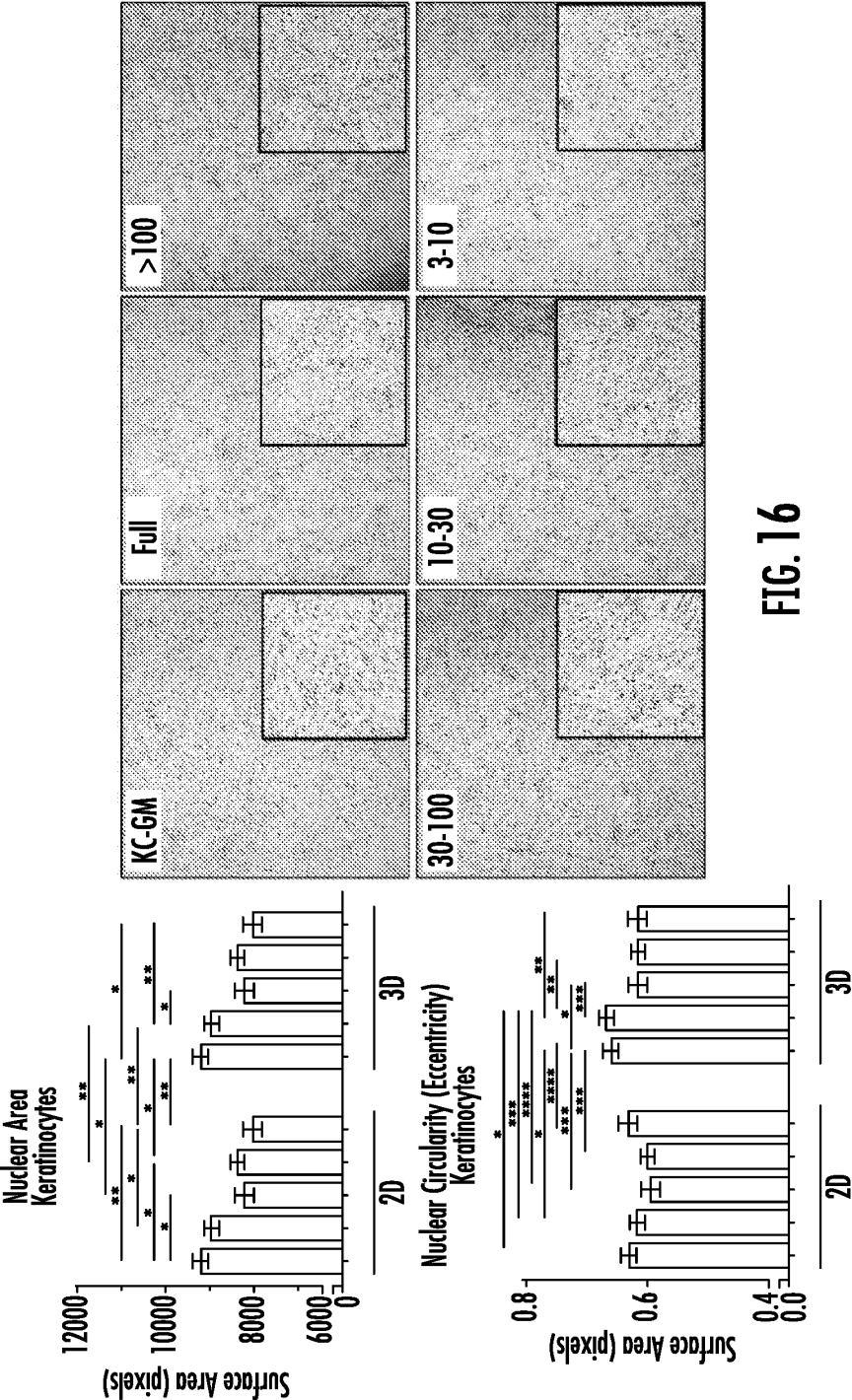
Gene Target		Relative Expression						
Migration								

FIG. 14E

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**FIG. 15**

Comparative KC Morphological Changes with/without DiI-labeled EVs: ASC-EVs were isolated from both 2D and 3D systems, labeled with a lipophilic dye, DiI (red), and dosed into KC-GM at 250j.tg/mL for treatment of KCs and assessment of morphological changes. KC morphology under transmitted light (top row), low magnification (20x) of fluorescent images of KCs with phalloidin (green) and Hoechst (blue) to depict formation of cell sheets in 3D-EV treated group, and high magnification (60x) of DiI-labeled EVs (red) to assess perinuclear localization of EVs. Control KC group (left column) compared to 2D-EV treated (middle column) and 3D-EV treated (right column). Scale bar for 20x images = 100µm, for 60x images = 25µm.



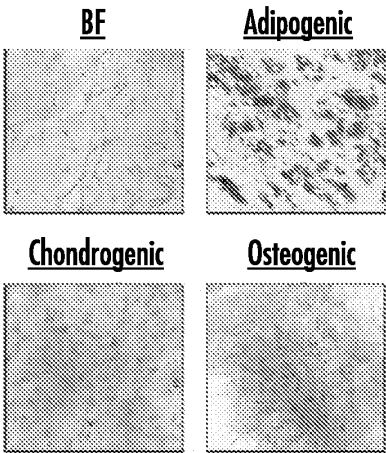


FIG. 17A

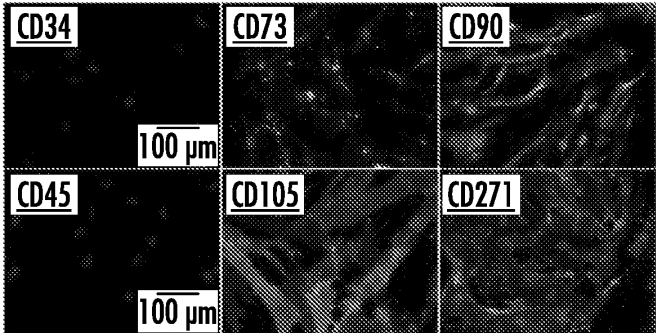


FIG. 17B

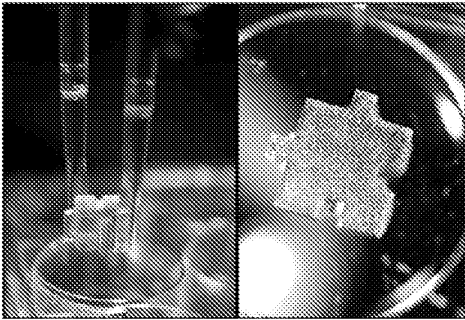


FIG. 17C

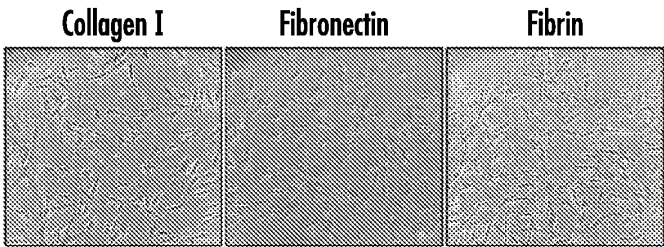


FIG. 17D

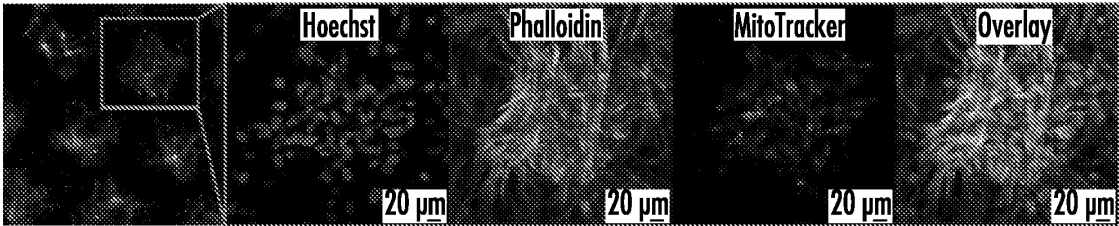
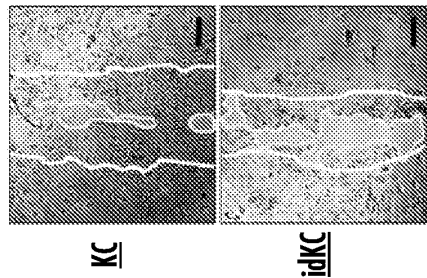
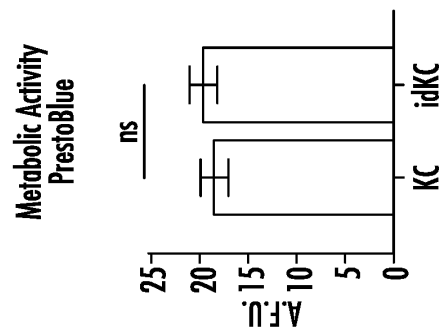
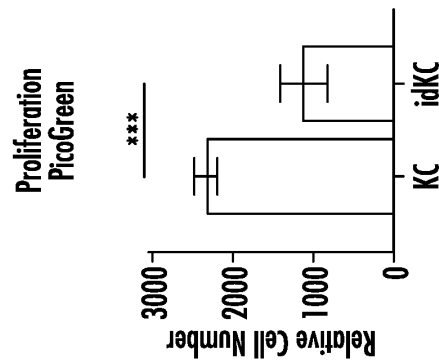
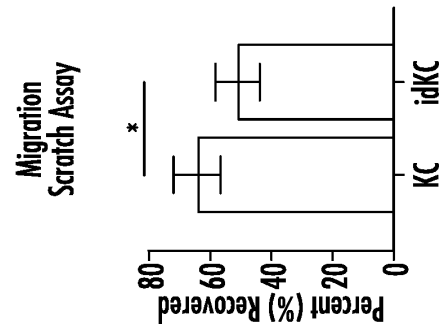
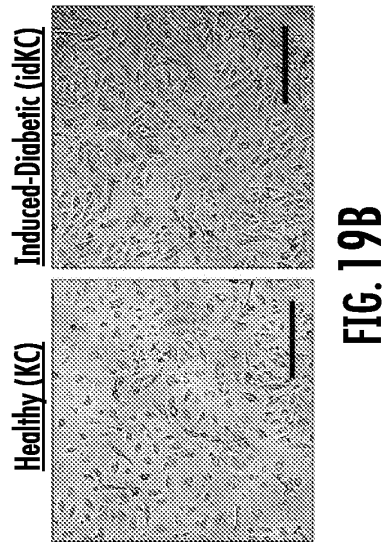
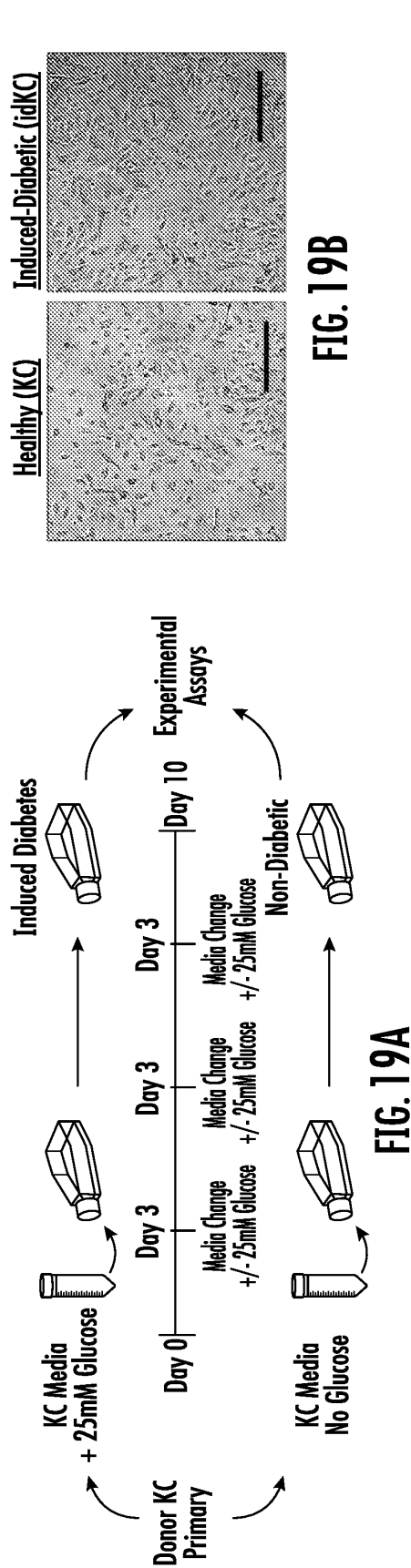


FIG. 18



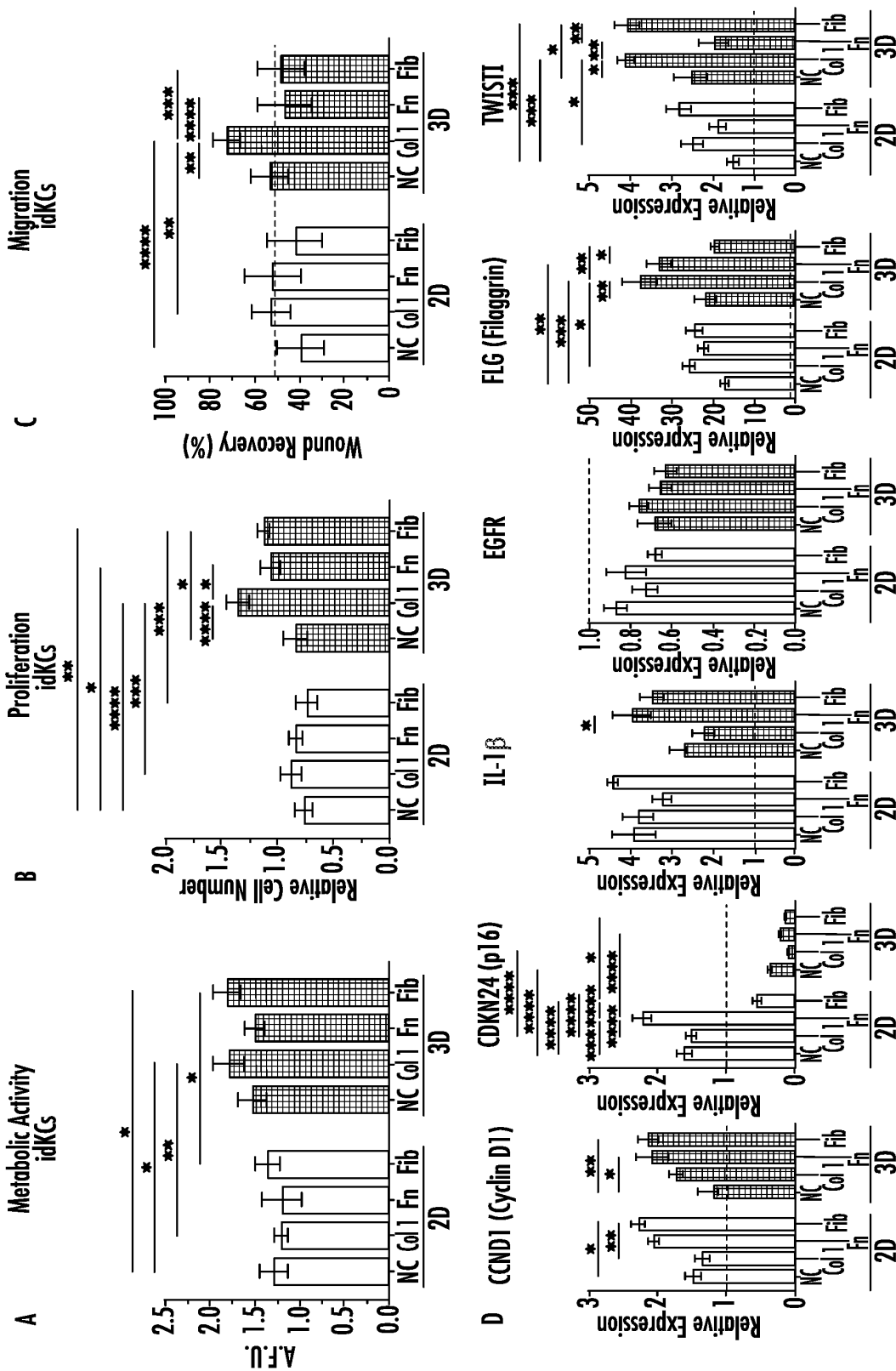


FIG. 20

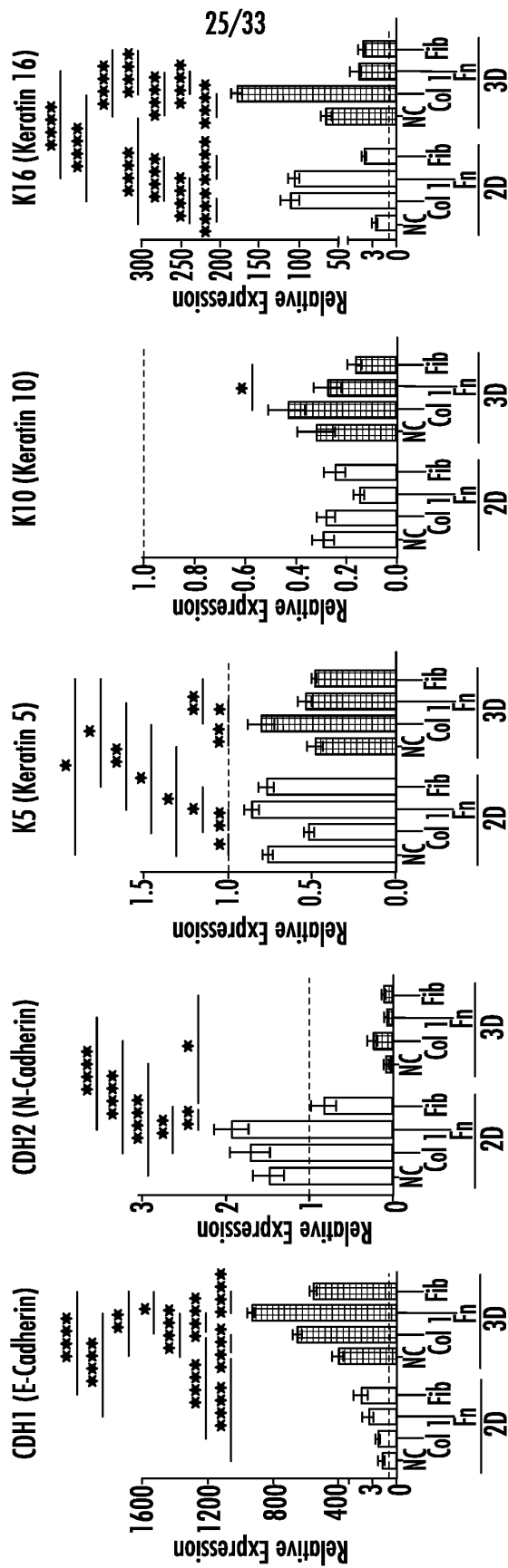
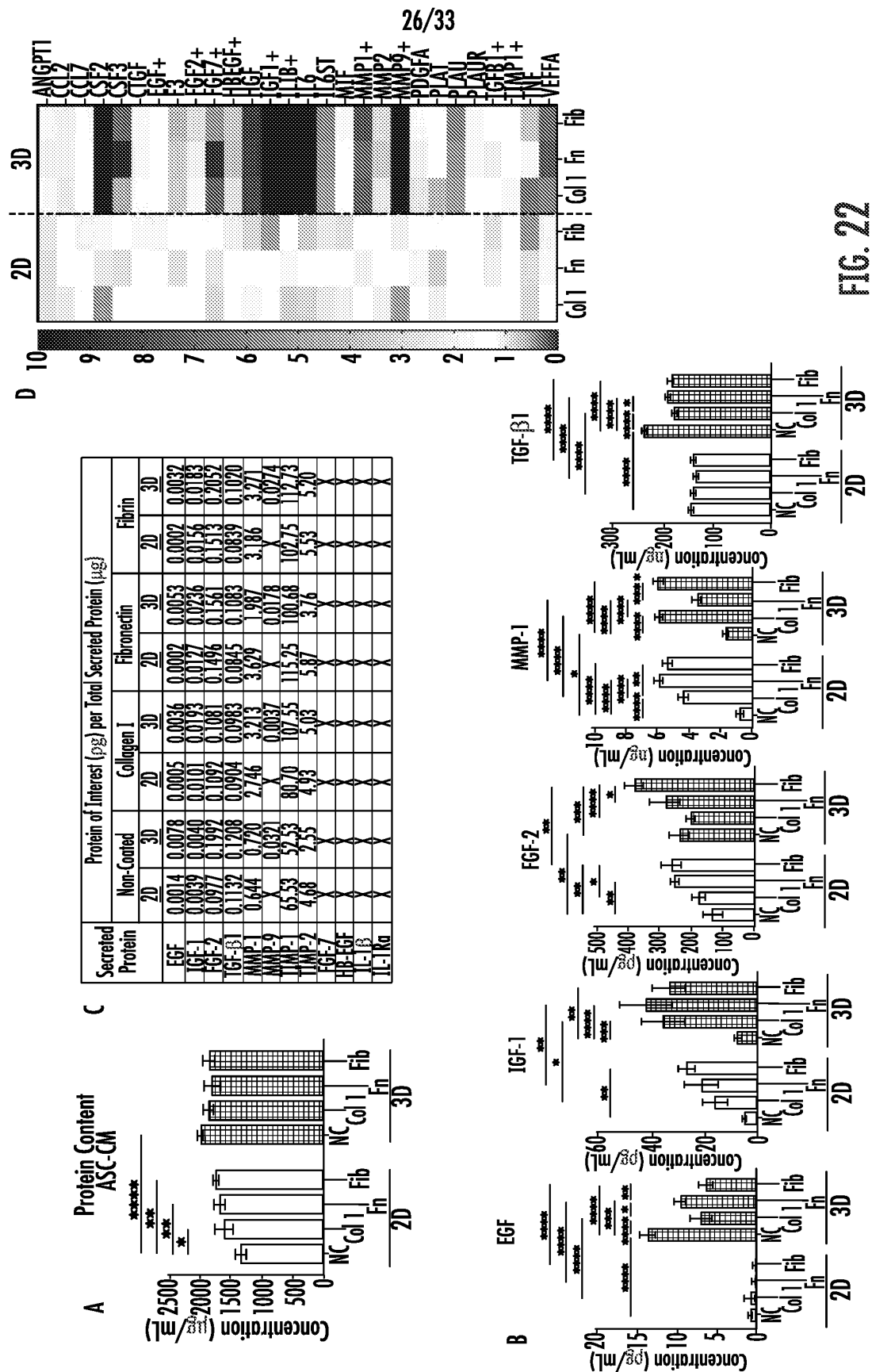


FIG. 21



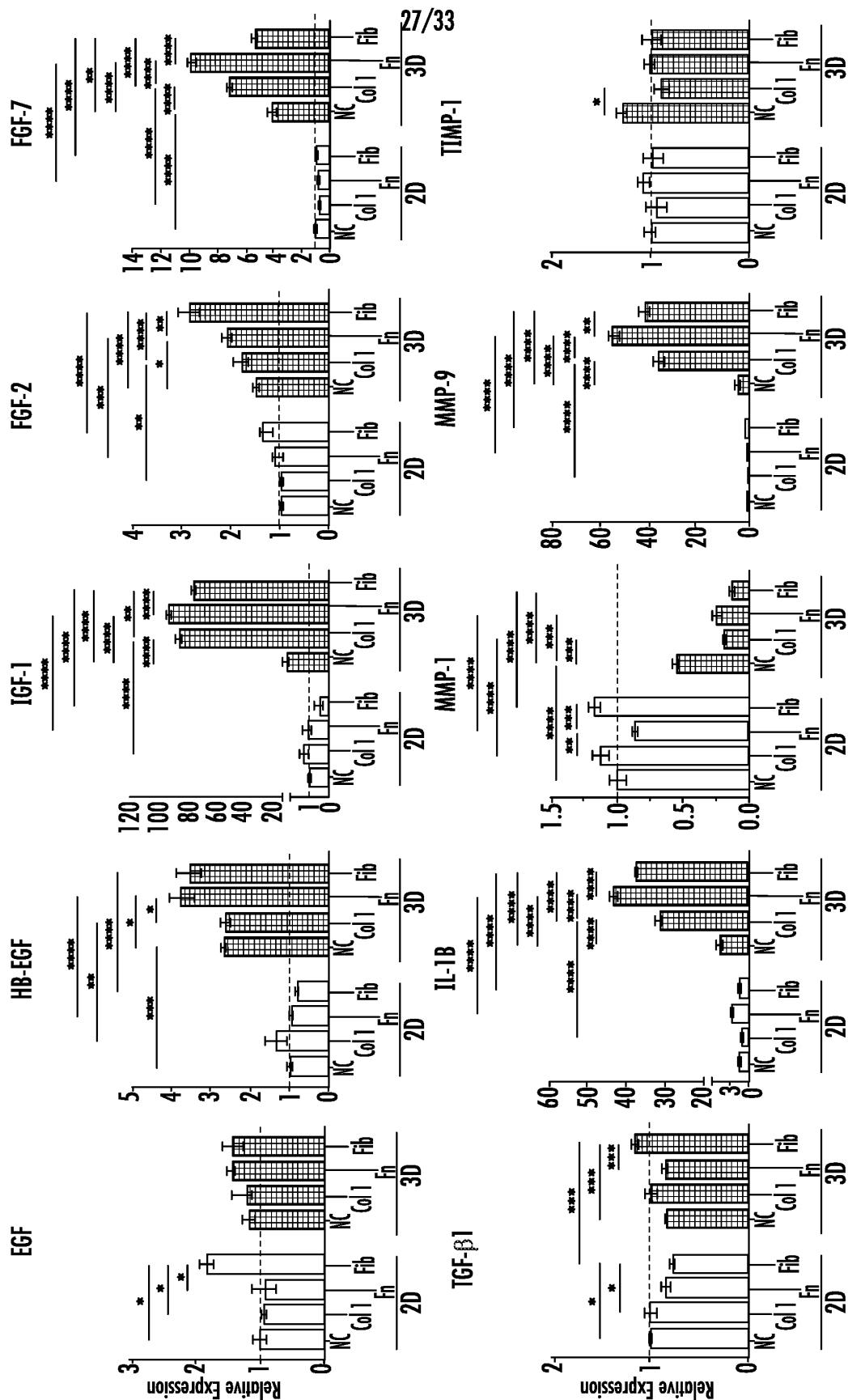


FIG. 23

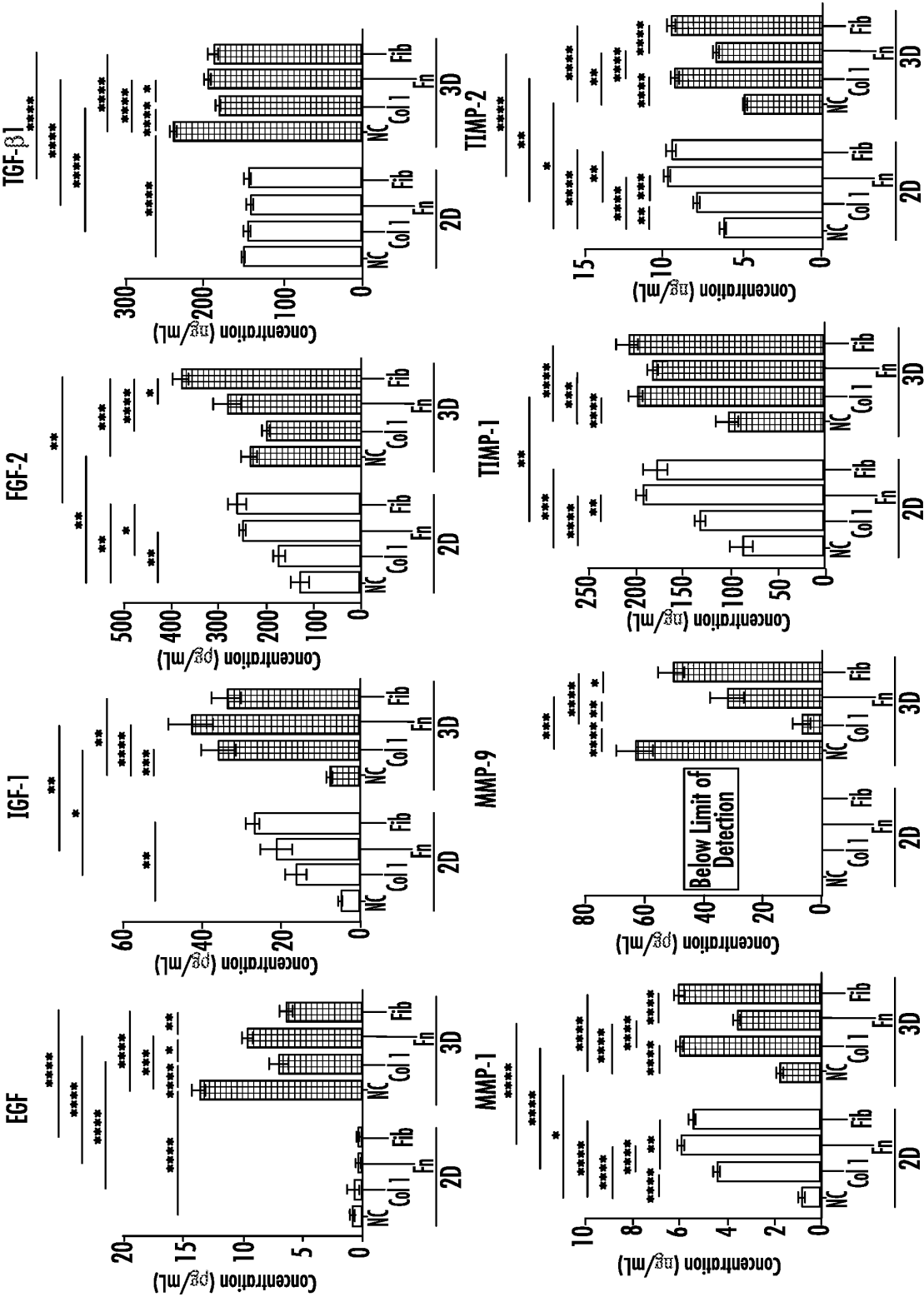
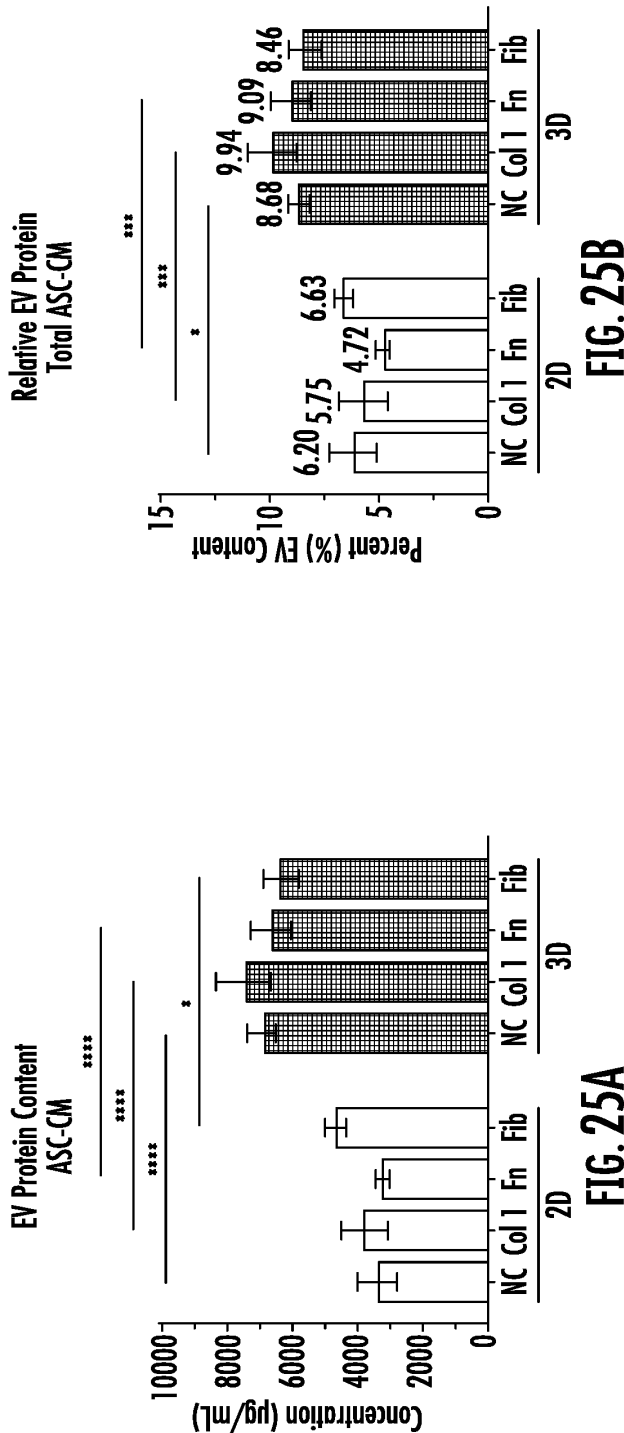
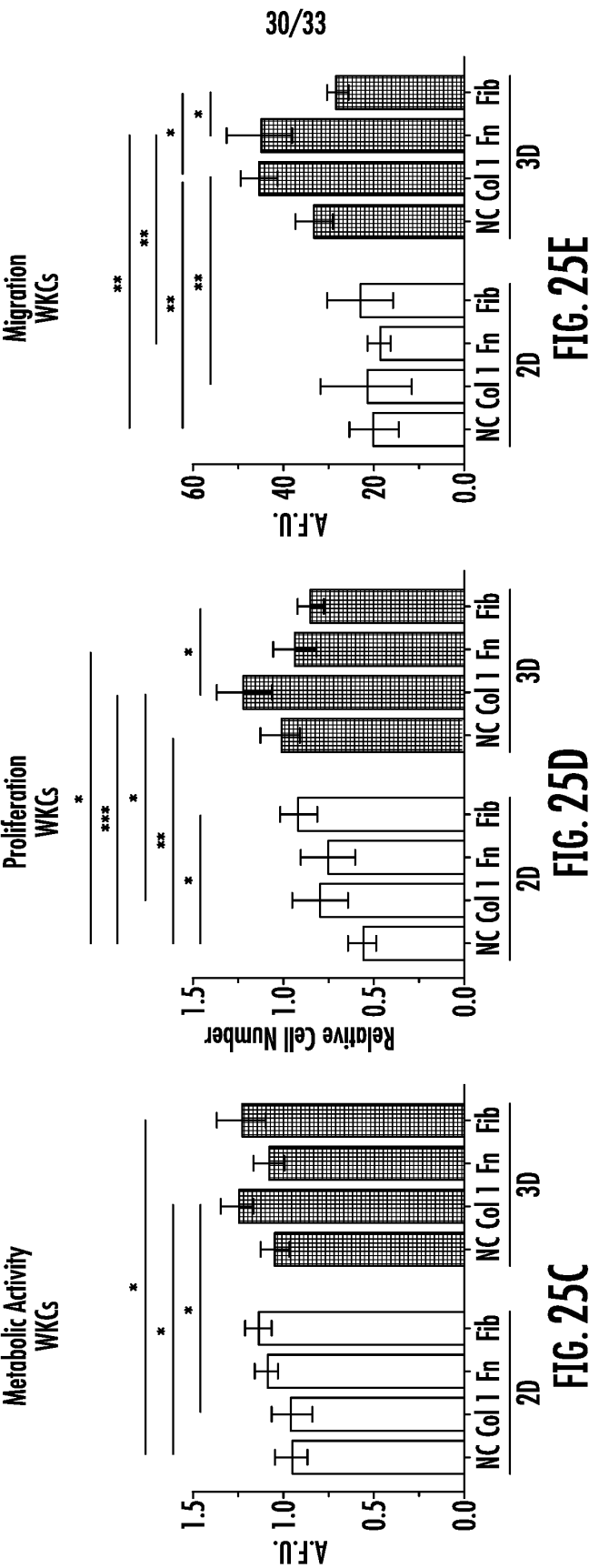


FIG. 24





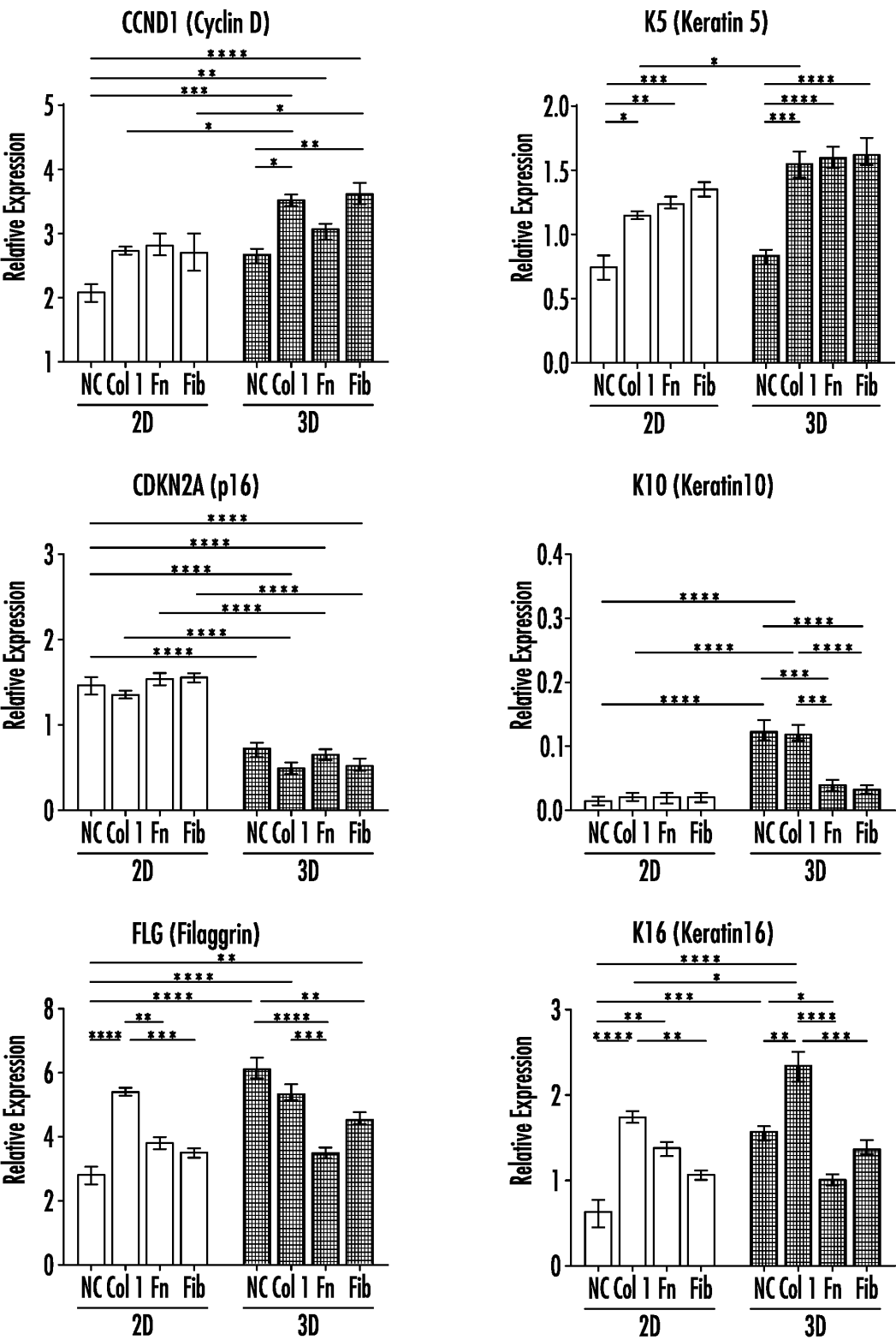


FIG. 25F

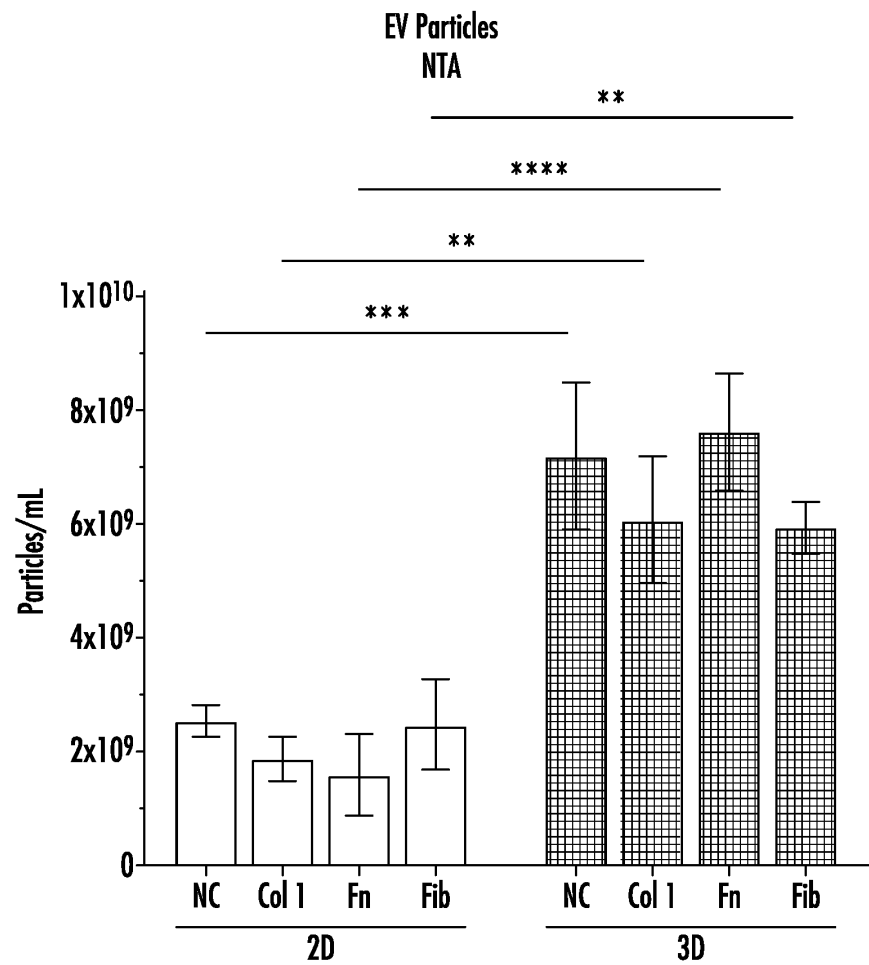


FIG. 26

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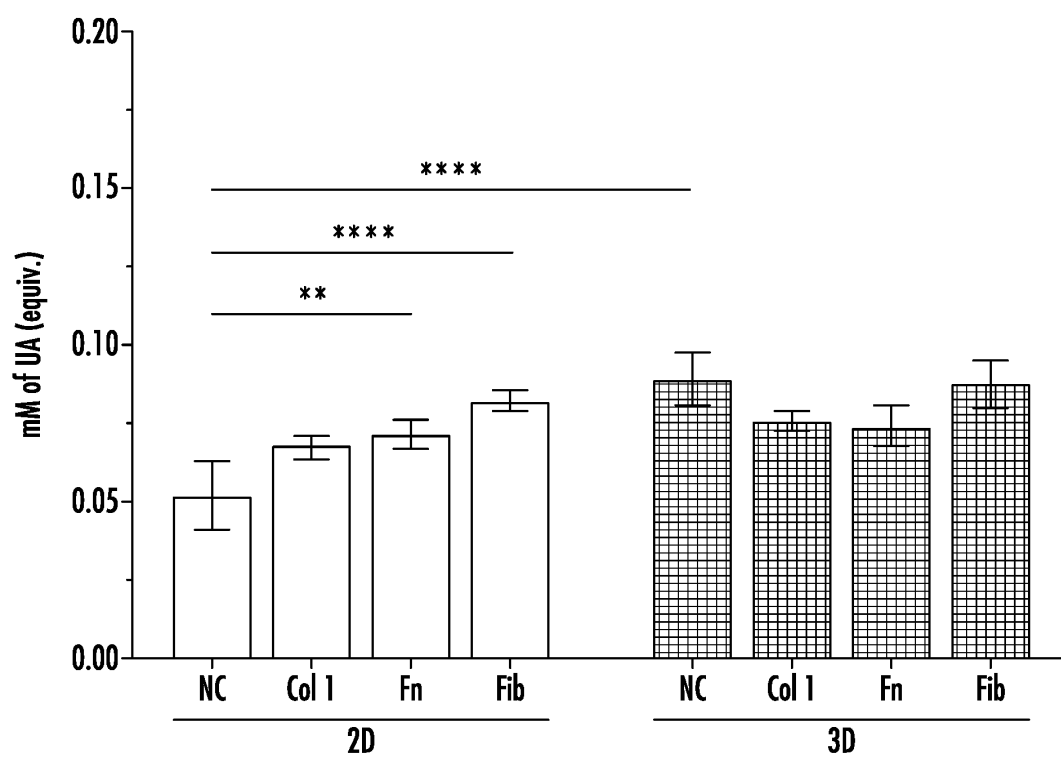


FIG. 27