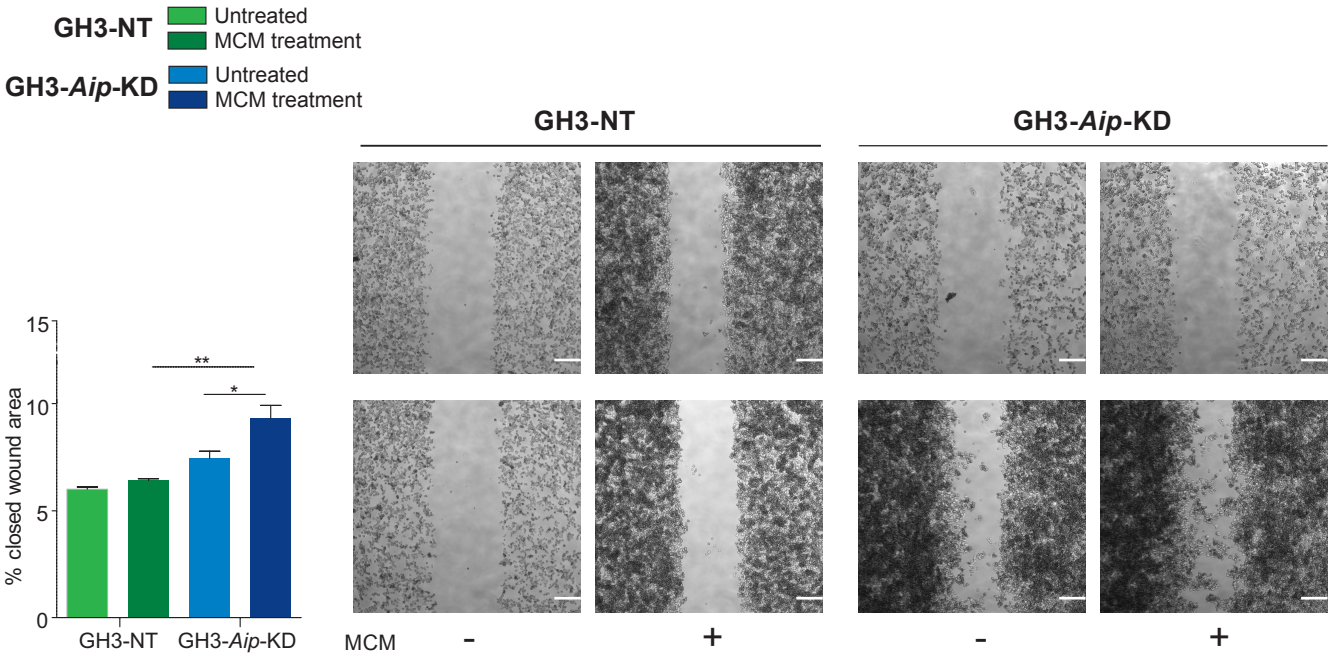SUPPLEMENTARY FIGURE 4