

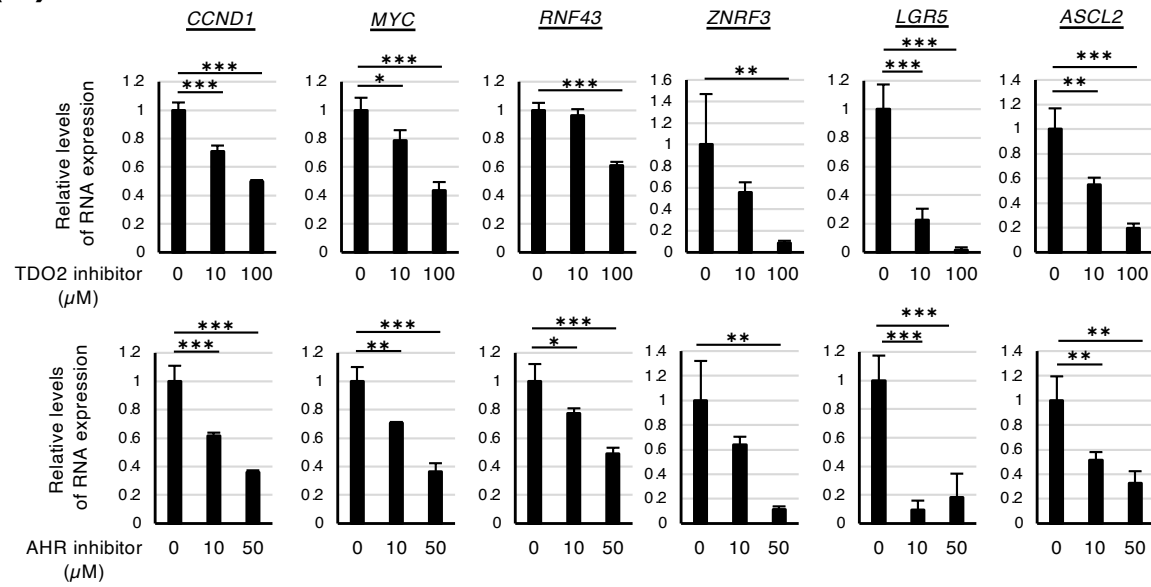
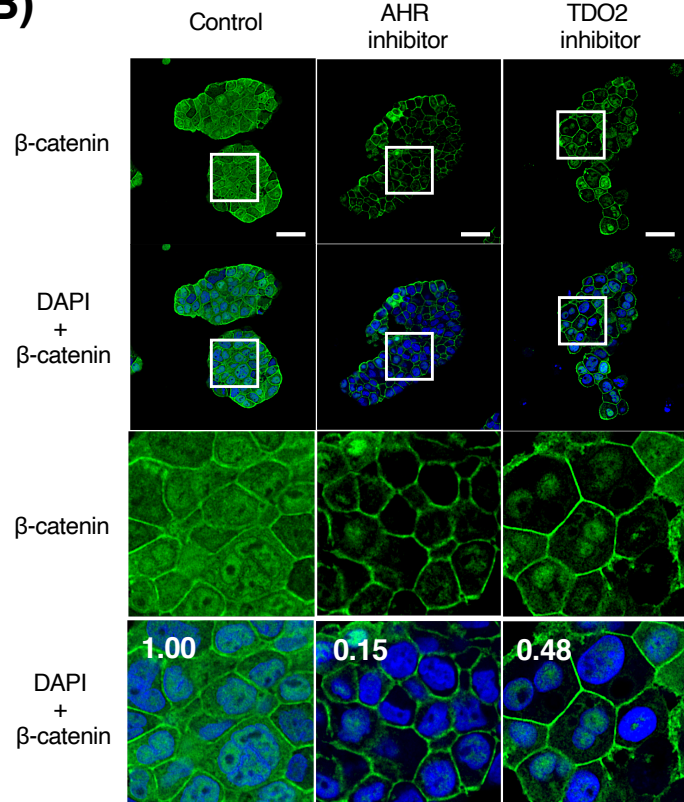
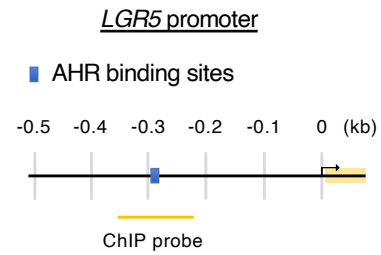
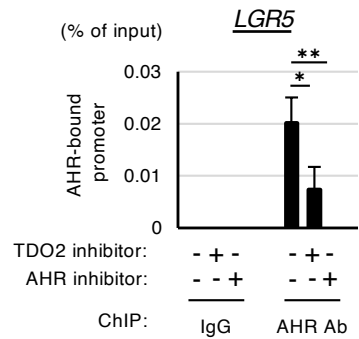
(A)**(B)****(C)****(D)**

FIGURE S6 The TDO2-AHR pathway is required for transactivation of *LGR5* and Wnt signaling in colon cancer spheroids. A, qPCR analyses of representative Wnt target genes in the metastatic spheroids (CRC-29M) after treatment with the indicated concentration of the inhibitor of (upper panels) TDO2 or (lower panels) AHR for 96 hrs. B, Immunostaining of the spheroids (CRC-29M) with β -catenin in the presence of the indicated inhibitor for 96 hrs. Nuclei were counterstained with DAPI. Relative quantification values of nuclear β -catenin were shown in the bottom columns. The bar represents 25 μ m. C, Schematic representation of predicted AHR binding sites in the promoters of *LGR5*. D, ChIP analyses of the AHR-bound promoters of the *LGR5* gene in spheroid cells (CRC-29M) treated with the TDO2 inhibitor (100 μ M) or AHR inhibitor (50 μ M) for 96 hr. Enrichment over input (% input) was measured by qPCR. Values represent the mean \pm s.d. * P < 0.05, ** P < 0.01, *** P < 0.001.