

Figure S1

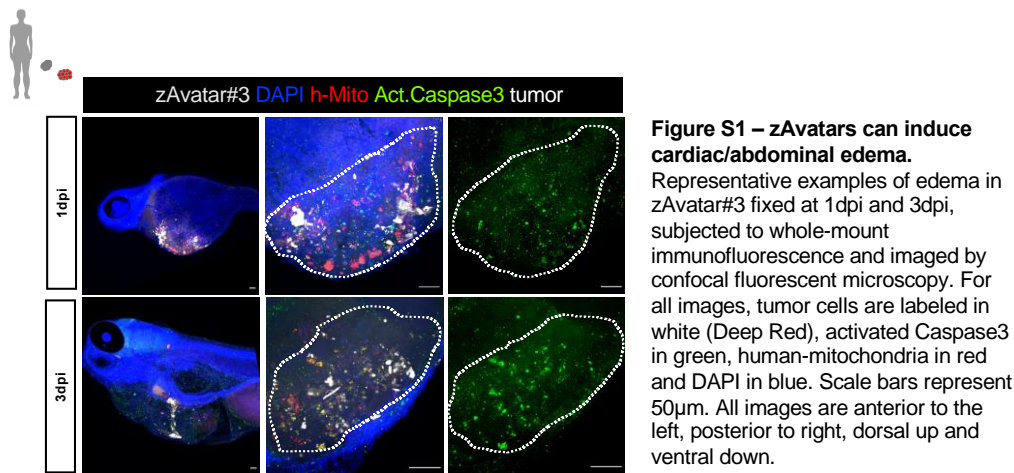


Figure S2

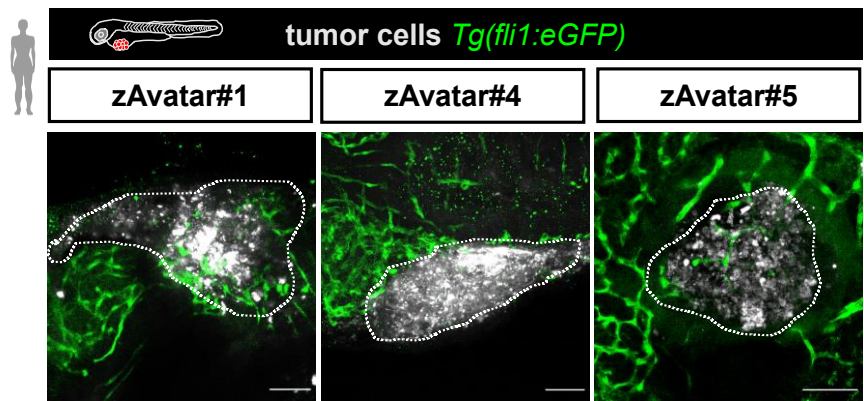


Figure S3

Giemsa Slide ID	Dx extended	Cytopathology									zPDX	
		cellularity	cohesiveness	naked nuclei	background					other comments	engraftment	angiogenesis
					nuclear tangles	necrosis	stromal fragments	inflammatory cells	apoptotic debris			
#1	PDAC	-	-	-	-	-	-	-	-		70%	yes
#2	PDAC	high	cohesive	20-50%	few	minimal	few	abundant (macrophages)	few	polygonal cells predominant	42%	yes
#3	PDAC	low	poorly cohesive	abundant	abundant	moderate	abundant	abundant (macrophages)	abundant	a lot of cell debris	edema	-
#4	ampullary type	moderate	cohesive	few (<10%)	few	minimal	few	few	few	columnar cells predominant	42%	yes
#5	ampullary type	high	cohesive	20-50%	few	minimal	few	few	few	marked cellular atypia		
#6	distal cholangiocarcinoma	moderate	poorly cohesive	20-50%	moderate	moderate	few	few	moderate	marked cellular atypia, bacteria	edema	-

Figure S3. Cytopathologic features of human pancreatobiliary tumors used to establish zAvatars. After dissociation from the original tumor samples, smears were performed and stained with May-Grunwald-Giemsa for quality control analysis. Cellularity, cohesiveness, necrosis and presence of inflammatory were some of the parameters analyzed. We were not able to analyze smears for patient#1.

Table S1. Stock and working concentrations in patients of the antineoplastic drugs used.

Drug	Stock concentration	Working concentration
5-FU	50 mg/mL	426.2 μ M
Oxaliplatin	5 mg/mL	8.1 μ M
Irinotecan	20 mg/mL	8 μ M
Folinic Acid	10 mg/mL	18.5 μ M
Gemcitabine	40 mg/mL	160 μ M
Paclitaxel	6 mg/mL	475 μ g/mL

Table S2. Composition of media used for the generation of zAvatars.

	Reagent	Supplier	Final concentration
Collection medium	Advanced DMEM/F-12	Gibco	-
	Penicillin-Streptomycin	Sigma-Aldrich	100U/mL
	Amphotericin B solution	Sigma-Aldrich	100 μ g/mL
	Kanamycin solution	Sigma-Aldrich	100 μ g/mL
	Gentamicin solution	Sigma-Aldrich	500 μ g/mL
	Amoxicillin/Clavulanic acid	Clavepen	220 μ g/mL
	Metronidazole	Braun	80 μ g/mL
Mix 1	DMEM F12	Gibco	
	HEPES	ThermoFisher	1%
	Glutagro supplement	Corning	1%
	FBS (fetal bovine serum)	Gibco	40%
	Primocin	Invivogen	100 μ g/mL
	Anoikis inhibitor	Sigma-Aldrich	10 μ M
	Putrescine	Sigma-Aldrich	10 μ g/mL
	p38 inhibitor	Sigma-Aldrich	10 μ M
	Epidermal Growth Factor (EGF)	PeproTech	50ng/mL
	N-acetylcysteine	Sigma-Aldrich	1mM
	Insulin-transferrin-selenium	Corning	1%
	Nicotinamide	Sigma-Aldrich	10mM
Mix2	Ethylenediaminetetraacetic acid (EDTA)	Sigma	2mM
	Liberase TM	Roche	50ug/mL
	DNase	ThermoFisher	5U/mL
	Cell tracker Deep Red	Life Technologies	1 μ L/mL