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université
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Inserm

Institut national
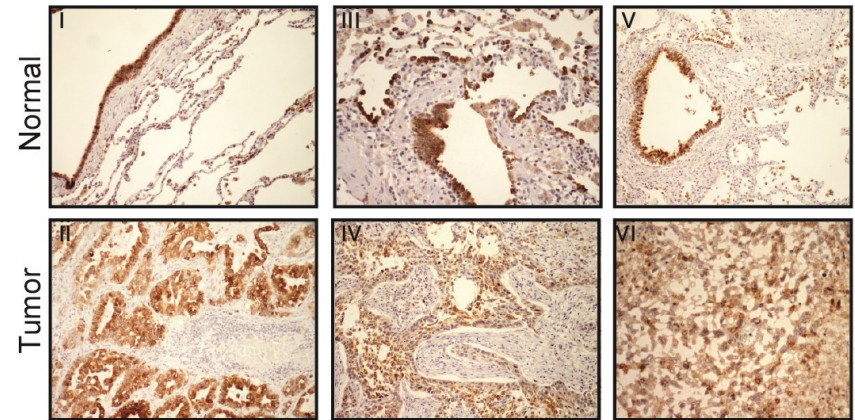de la santé et de la recherche médicale

SFR
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Anterior Gradient 2 (AGR2) levels in lung tissues

a
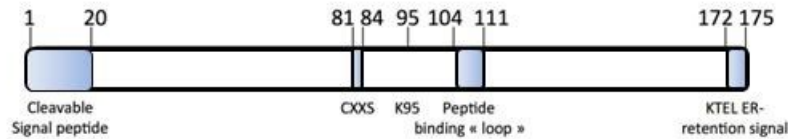
Primary structure of the AGR2 protein: The identified functional domains and amino acids implicated in regulation of its function are indicated by blue shaded boxes.

b

		Age	Sex	Grade	AGR2 intensity			Cumulative, %		
					Low	Moderate	High	Low	Moderate	High
Large cell carcinoma										
	1	49	F	IIIA			1			
Squamous cell carcinoma								16.6	66.6	16.6
	1	73	M	IIIA		1				
	2	57	M	IIIA	1					
	3	62	M	IIIA		1				
	4	60	M	IIIB			1			
	5	53	M	IIIB		1				
	6	58	M	IIIA		1				
Adenocarcinoma								14.3	0	85.7
	1	52	F	IIIA			1			
	2	59	M	IIIA			1			
	3	38	F	IIIB			1			
	4	49	M	IIA			1			
	5	60	M	IIIA			1			
	6	59	F	IIB	1					
	7	58	M	IIIA			1			
Total cases NSLCC								14.3	28.57	57.14

AGR2 overexpressed in lung cancer tissues

Organotypic culture of human bronchial epithelial cells
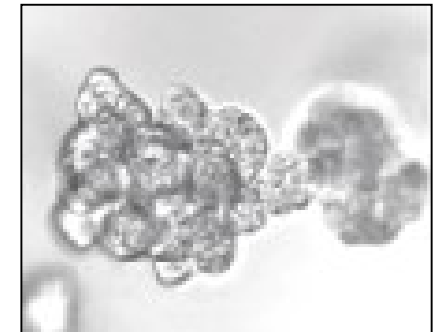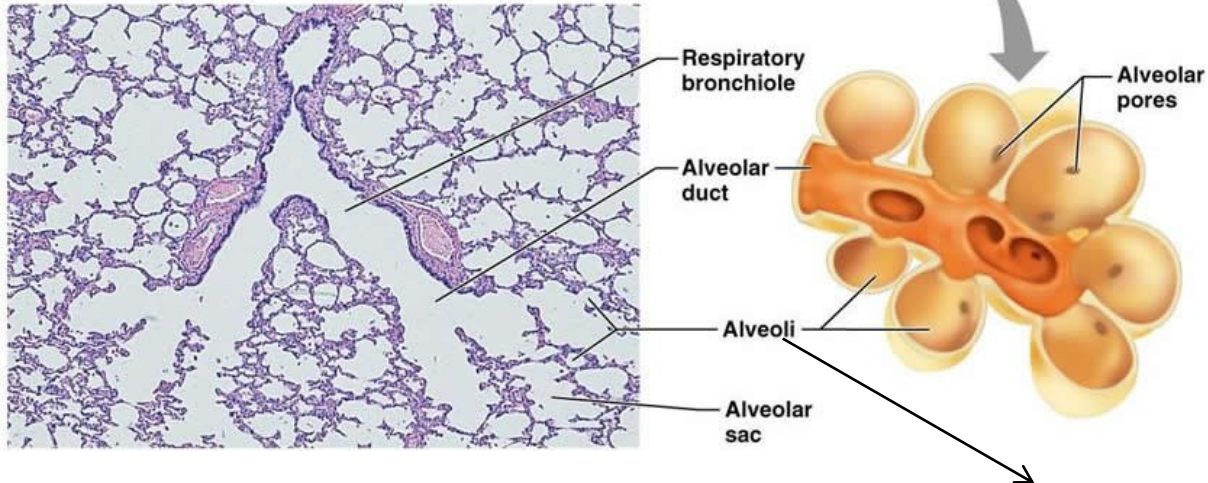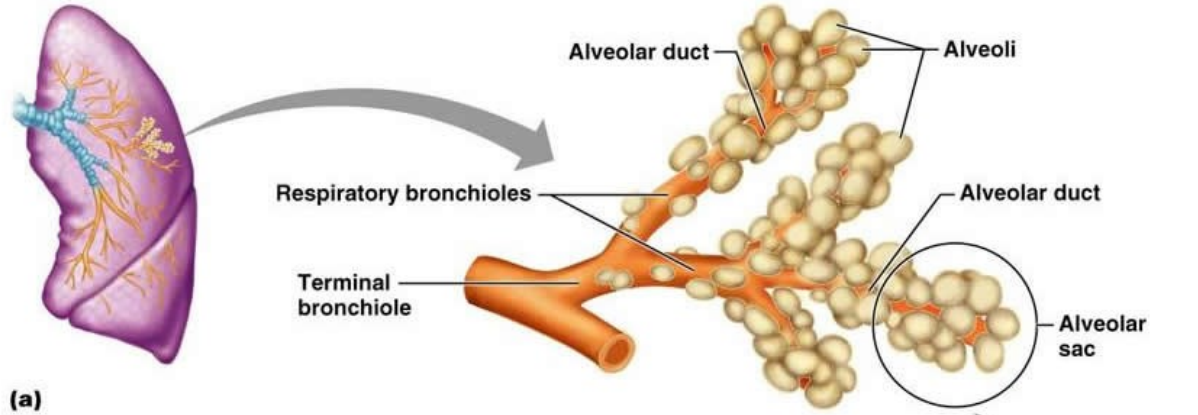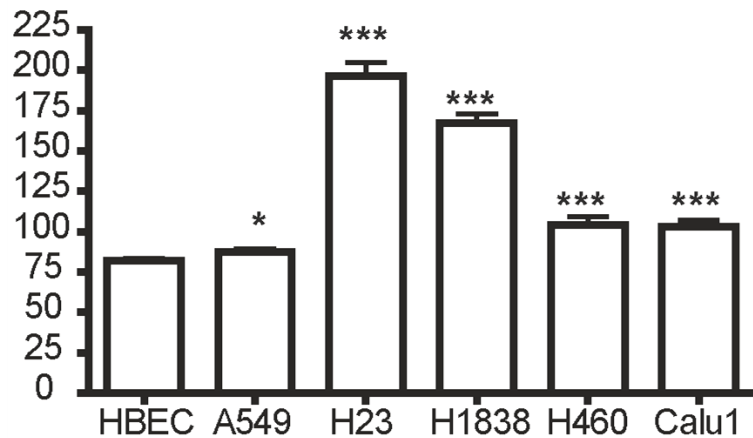
AGR2 levels in lung organoids
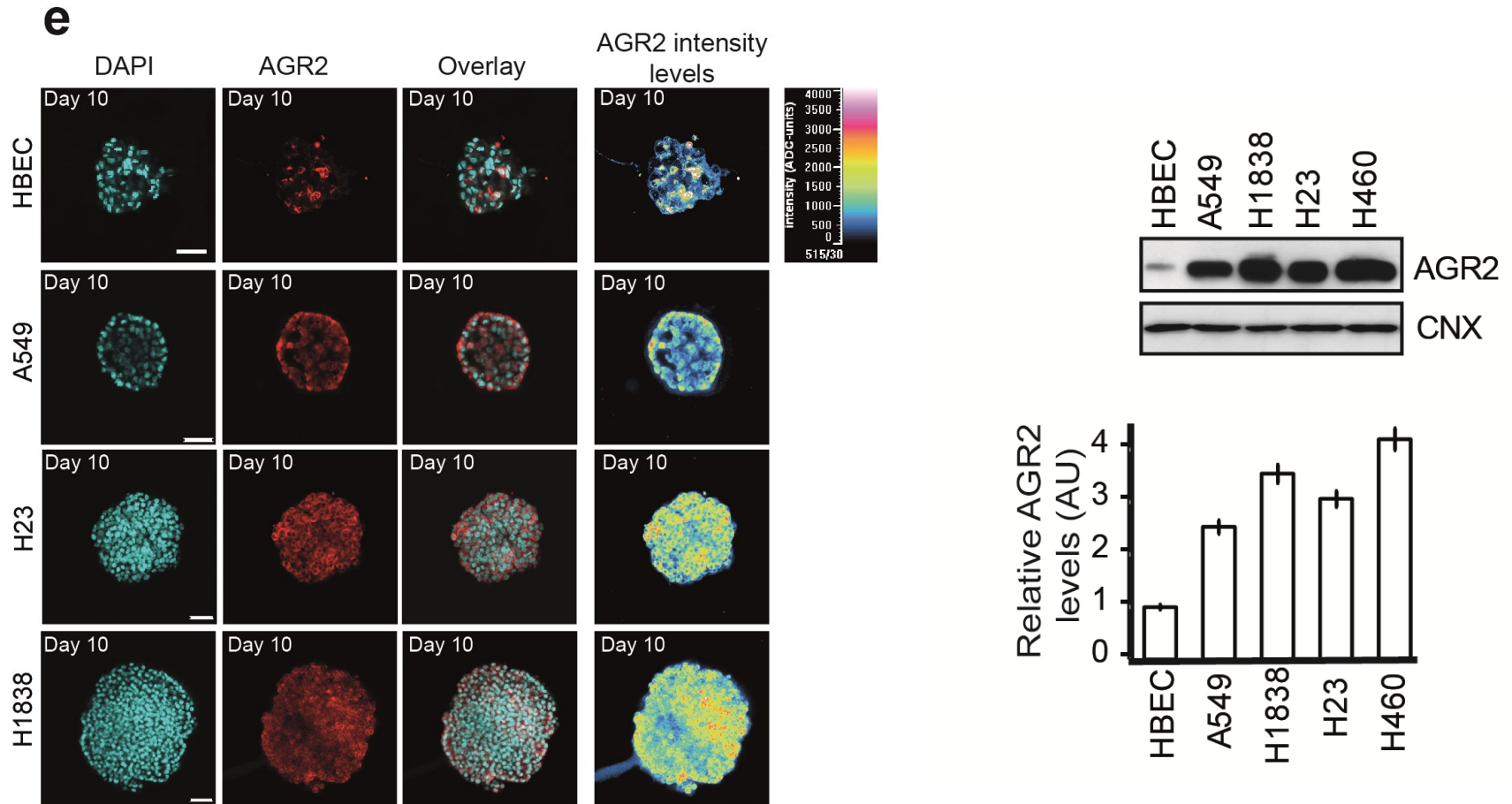
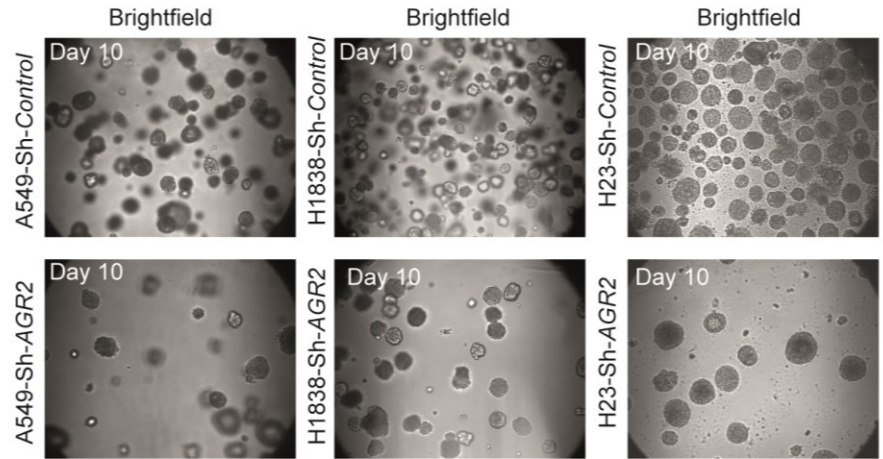AGR2 overexpressed in lung cancer organoids

Knocking down AGR2 expression
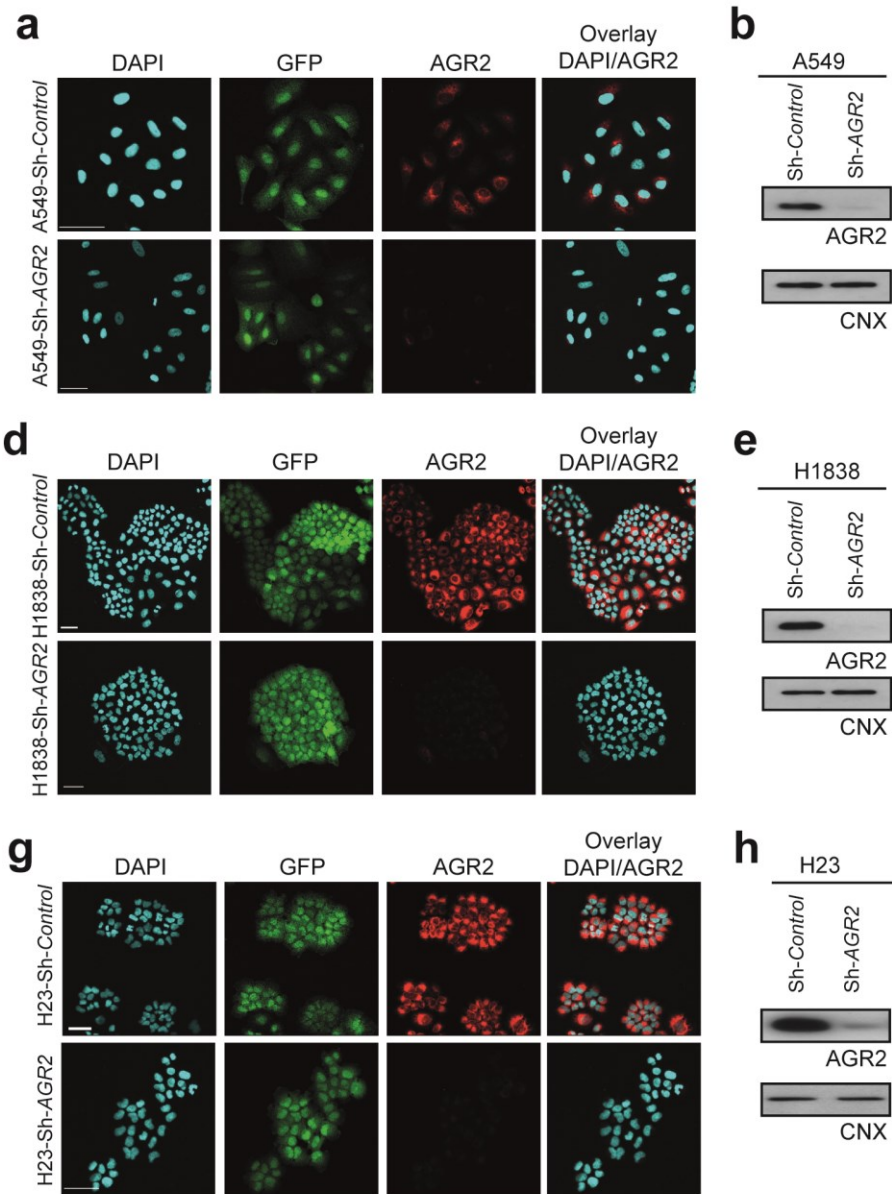
Knocking down AGR2 expression decreases organoid formation
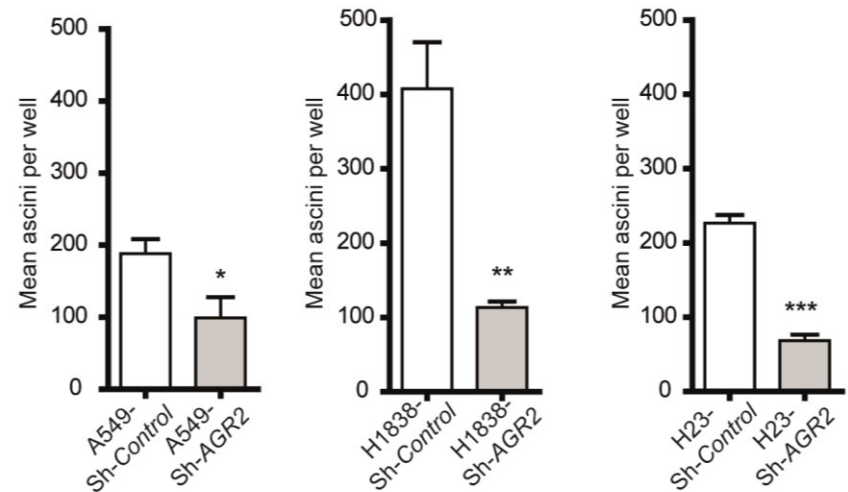
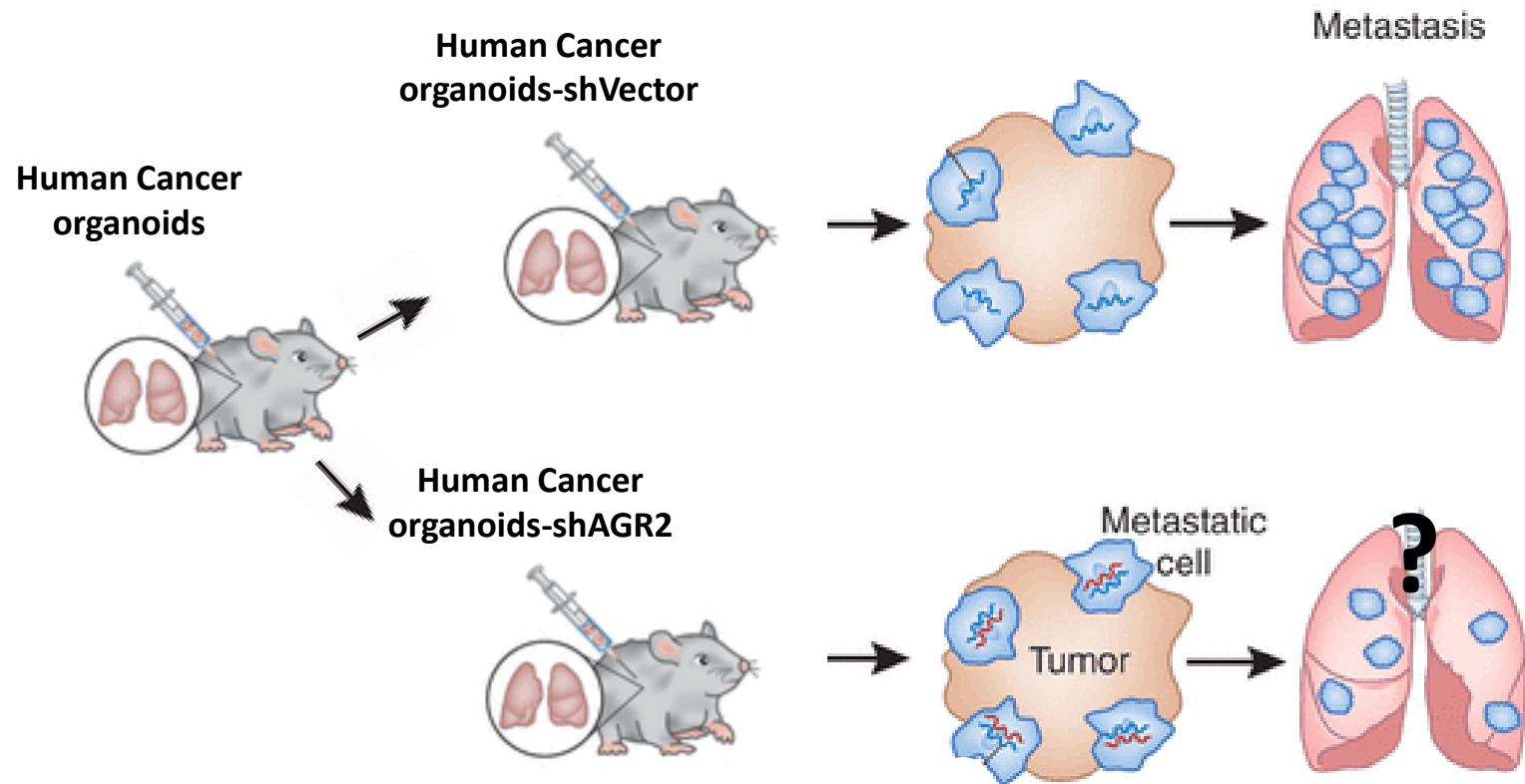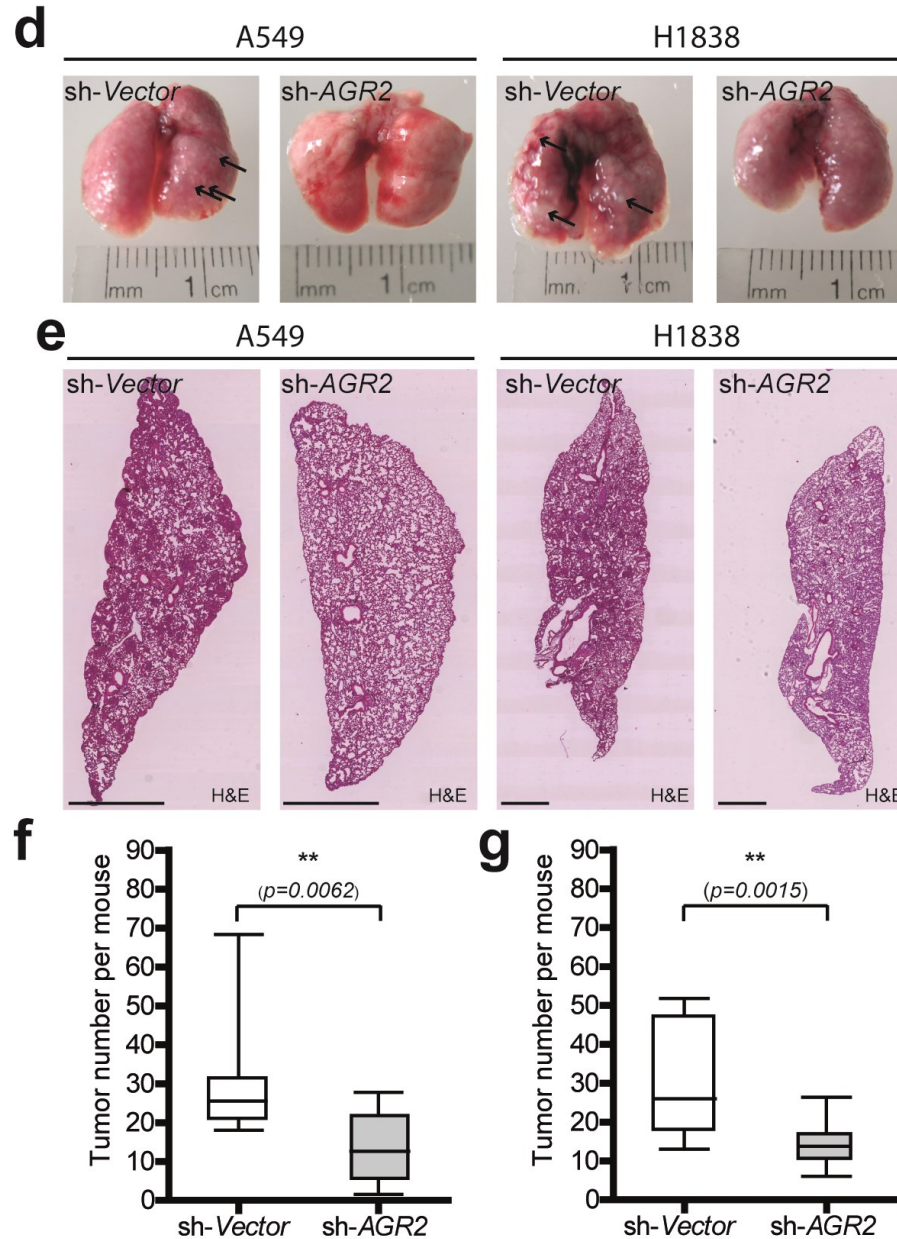# Mouse Orthotopic Lung Cancer Model

Human Cancer organoids

Human Cancer organoids-shVector

Human Cancer organoids-shAGR2

Metastasis

Metastatic cell

Tumor

?

Knocking down AGR2 expression decreases tumorigenicity in vivo

d

A549

sh-*Vector*   sh-*AGR2*

H1838

sh-*Vector*   sh-*AGR2*

e

A549

sh-*Vector*   sh-*AGR2*

H1838

sh-*Vector*   sh-*AGR2*

H&E   H&E   H&E   H&E

f

Tumor number per mouse

** (p=0.0062)

sh-*Vector*   sh-*AGR2*

g

Tumor number per mouse

** (p=0.0015)

sh-*Vector*   sh-*AGR2*

# Knocking down AGR2 expression decreases organoids formation

Serum AGR2 as an early diagnostic and postoperative prognostic biomarker of human lung adenocarcinoma

Kyukwang Chung[a,b], Noritoshi Nishiyama[a], Shotaro Yamano[b], Hiroaki Komatsu[a,b], Shoji Hanada[a,b], Min Wei[b], Hideki Wanibuchi[b,*], Shigefumi Suehiro[a] and Anna Kakehashi[b]
[a]Department of Thoracic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan
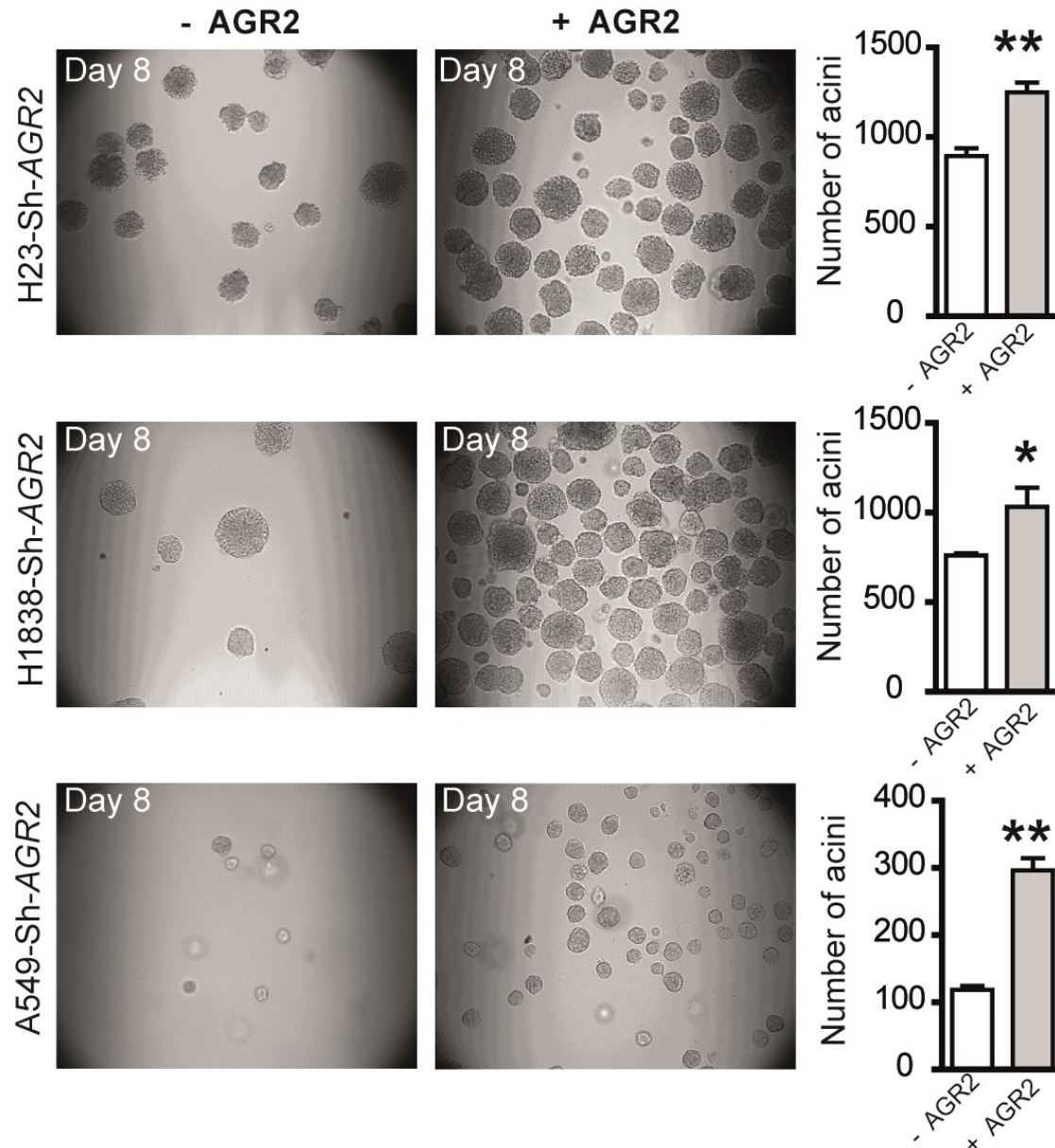[b]Department of Pathology, Osaka City University Graduate School of Medicine, Osaka, Japan
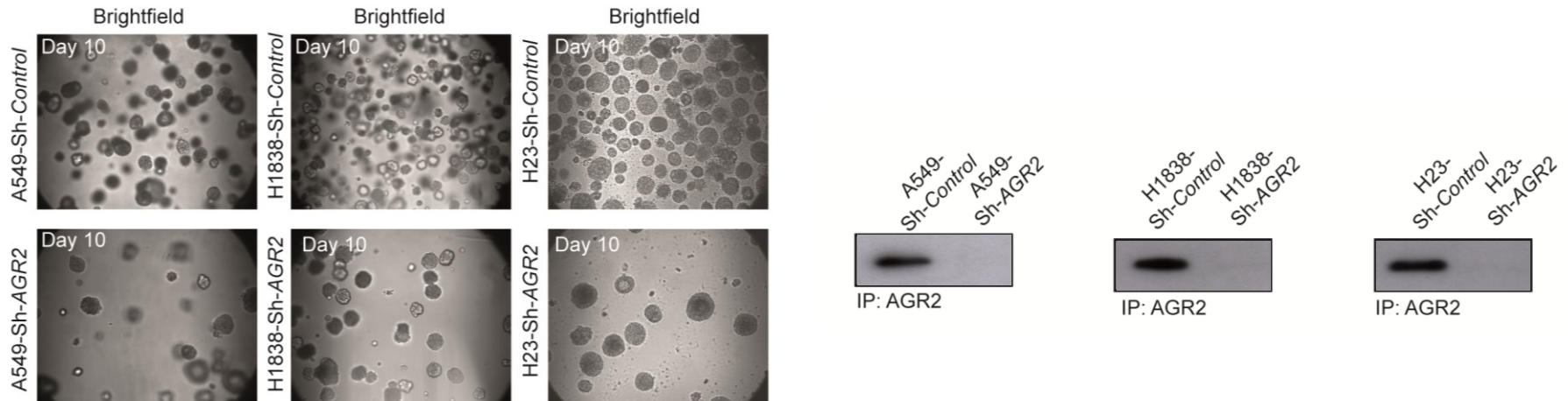
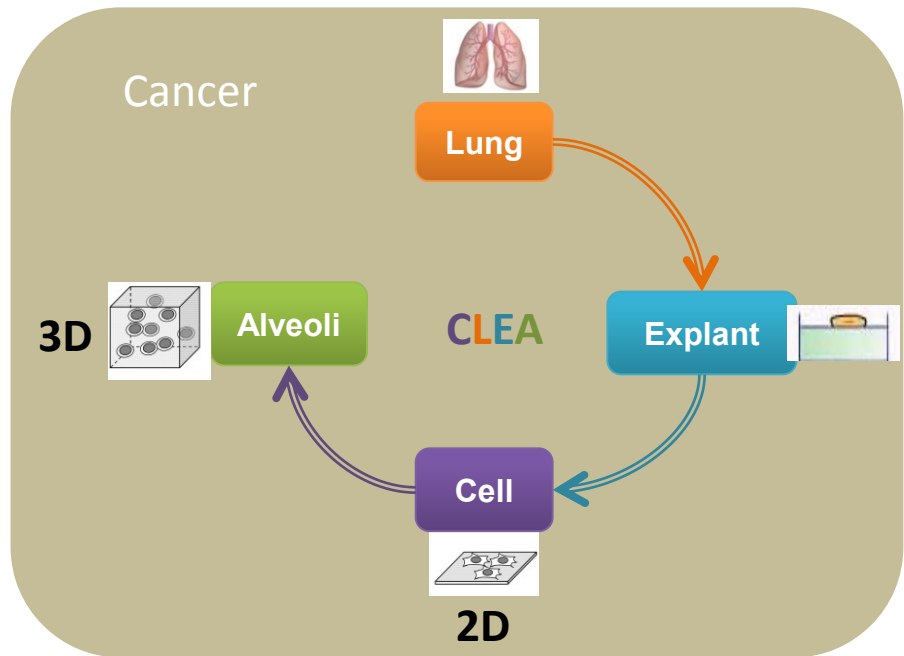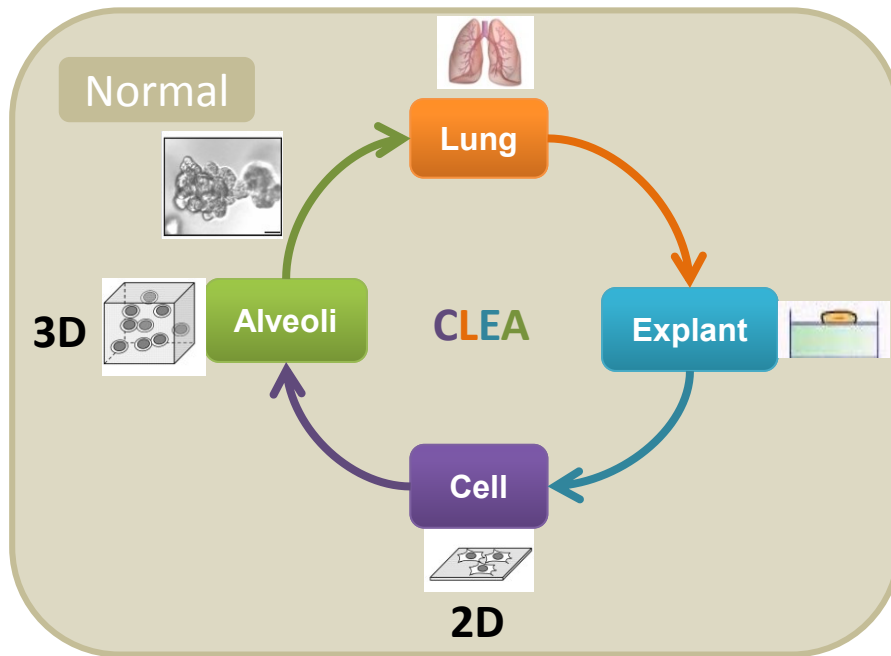## AGR2 secreted and organoids formation?

AGR2 secreted modulates organoid formation/tumorigenicity

Conclusion

"Cell Lung Explant Alveoli" = CLEA

Candidate or molecules of therapeutic interest on the regeneration, differentiation, morphogenesis and tumorigenesis of human respiratory epithelium

Role of AGR2 secreted in tumorigenicity, suggesting that this protein could be an interesting target for the successful treatment of lung cancer.

Acknowledgements

FD lab

Collaborators

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- **Kasia A. Rejniak:** Moffit cancer center, Tampa, USA

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