

Kholle du vendredi 10 Mai - Métabolisme des cellules et cancer

Dans ce sujet, on s'intéresse à l'implication de certaines enzymes, en particulier celles du métabolisme du glucose, dans la formation de tumeurs. En effet, de nombreuses enzymes de la glycolyse ont, dans le cadre des cancers, des fonctions non-métaboliques[2], cruciales pour comprendre le développement des tumeurs.

1 Rappel - Le métabolisme du glucose

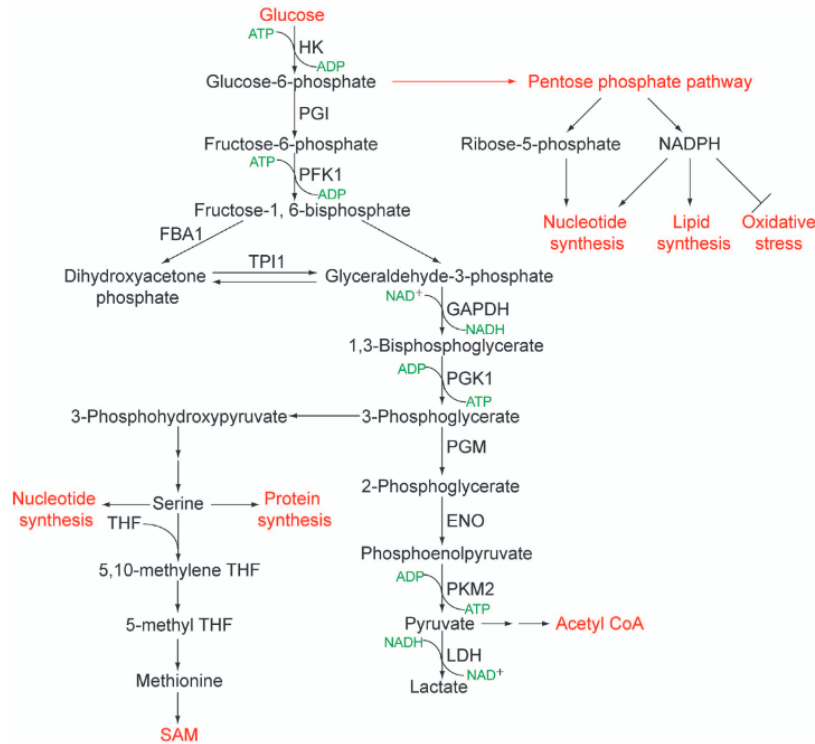


Figure 1. Overview the connection of glucose metabolism, pentose phosphate pathway, amino acid biosynthesis, and lipid synthesis. ENO, enolase; FBA1, fructose 1,6-bisphosphate aldolase 1; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; HK, hexokinase; LDH, lactate dehydrogenase; PFK1, phosphofructokinase 1; PGI, phosphoglucose isomerase; PGK1, phosphoglycerate kinase 1; PGM, phosphoglycerate mutase; PK, pyruvate kinase; THF, tetrahydrofolate; TPI, triosephosphate isomerase.

2 Implication de PGK1 dans le développement de tumeurs

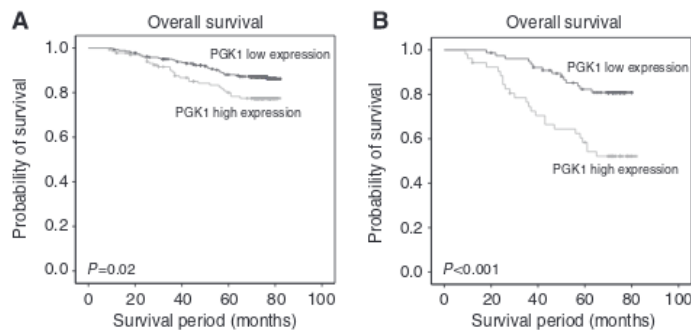


Figure 3. Kaplan-Meier analysis for survival based on PGK1 expression. (A) Survival curves showing the correlation of PGK1 with OS in breast cancer patients ($P=0.02$). (B) Overall survival based on PGK1 expression in patients treated with paclitaxel ($P<0.001$).

Question 1 - Que concluez vous de ce document ? (paclitaxel est un des médicaments utilisés en chimiothérapie.)[1]

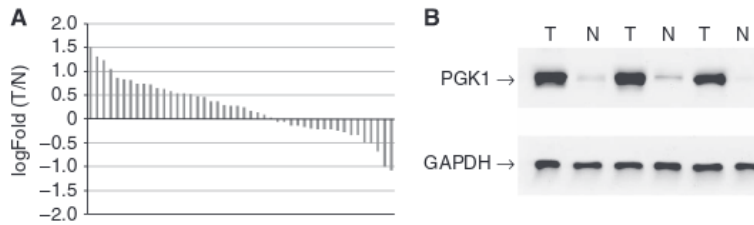


Figure 1. PGK1 elevated expression in fresh breast cancer tissues. (A) Histogram of PGK1 mRNA expression in breast cancer. The PGK1 mRNA expression was calculated by the $2^{-\Delta\Delta C_t}$ method, the relative expression in each patient was presented as the ratio of T (tumour tissue)/N (normal tissue). (B) Representative western blotting analysis of PGK1 expression in breast tissues. The levels of GAPDH were used as an internal control.

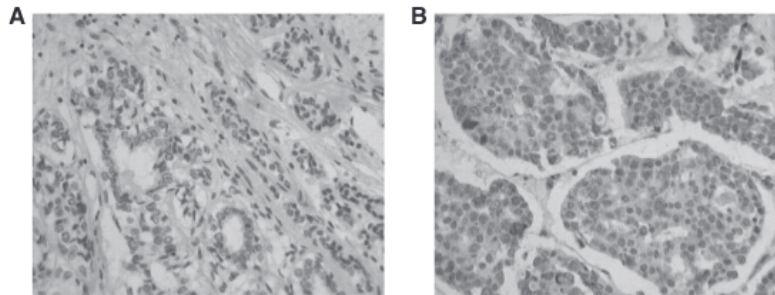


Figure 2. Immunohistochemical staining of PGK1 in breast tissues ($\times 400$). (A) PGK1 low-expression specimen (normal breast tissue). (B) PGK1 high-expression specimen (breast cancer tissue).

Question 2 - Que concluez-vous de ce document ?

3 L'hexokinase, impliquée dans le cancer ?

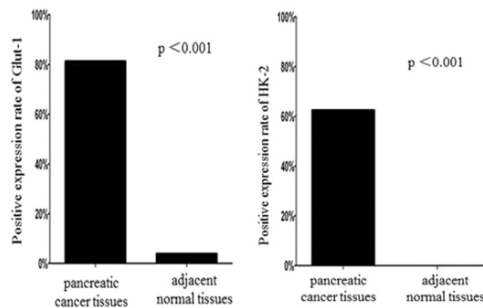


Figure 2. The positive expression rate of Glut-1 and HK-2 in pancreatic cancer tissue and adjacent normal tissue.

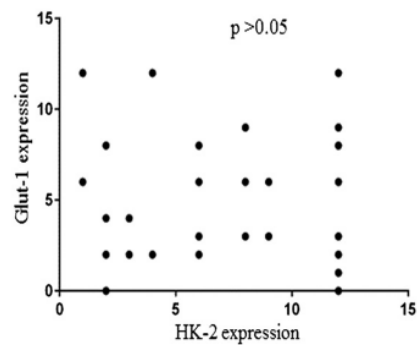


Figure 3. The correlation between Glut-1 expression and HK-2 expression.

Table 3. Associations Between HK-II Levels and Clinicopathological Variables in Pancreatic Cancer Patients

Patient Characteristics	Negative (-)	Positive (+ - +++)	Pvalue
Age			.870
≥60	13	21	
<60	5	9	
Gender			.252
Male	13	18	
Female	4	12	
Tumor size			.527
≤4 cm	11	21	
>4 cm	7	9	
Tumor location			.737
Head of pancreas	12	22	
Body and tail of pancreas	5	7	
Tumor histological type			>.05
Other types	4	7	
Ductal adenocarcinoma	14	23	
Tumor differentiation			>.05
II, III, III	6	17	
I, II	3	18	
Nerve infiltration			.881
Present	7	14	
Absent	10	16	
Vascular invasion			.441
Present	8	10	
Absent	10	20	
Local infiltration			0.513
Present	12	23	
Absent	6	7	
Lymph node metastasis			.551
Present	8	16	
Absent	10	14	
Tumor staging			.805
I-IIA	9	13	
IIB-IV	9	17	

Question 3 - Pensez vous que HK2 soit impliqué dans le développement du cancer ? Que pensez-vous de la table 3 ?

References

- [1] S Sun, X Liang, X Zhang, T Liu, Q Shi, Y Song, Y Jiang, H Wu, Y Jiang, X Lu, and D Pang. Phosphoglycerate kinase-1 is a predictor of poor survival and a novel prognostic biomarker of chemoresistance to paclitaxel treatment in breast cancer. *British Journal of Cancer*, 112(8):1332–1339, April 2015.
- [2] X Yu and S Li. Non-metabolic functions of glycolytic enzymes in tumorigenesis. *Oncogene*, 36(19):2629–2636, May 2017.

4 réflexions pour correction

4.1 PGK1

In conclusion, the identification of molecules associated with the response to chemotherapy might be important for predicting the efficacy of specific anti-neoplastic drugs and for the development of less empiric strategies regarding therapeutic choices. Our data demonstrated a significant correlation between PGK1 expression and poor prognosis in breast cancer. On the basis of the correlation between PGK1 expression and survival in breast cancer patients treated with paclitaxel, we suggested that PGK1 overexpression might be a prognostic biomarker of chemoresistance to paclitaxel treatment in breast cancer. Therefore, more studies are required to understand the precise role of PGK1 and to determine whether PGK1 may be used as a prognostic target. NB: le paclitaxel est un des médicaments utilisés en chimiothérapie.

4.2 HK2

Amener une réflexion sur l'étude des corrélations, si c'est significatif ou pas, parler de p-value (et pas de multiplication des expériences) Ccl de l'article : Our data show that Glut-1 and HK-II proteins are overexpressed in pancreatic cancer, but they have no correlation with clinicopathological features, survival and 18 F-FDG uptake. We guess that maybe there are other subtypes which contribute to a high rate of entry of the FDG into pancreatic cancer cells.

References

- [1] S Sun, X Liang, X Zhang, T Liu, Q Shi, Y Song, Y Jiang, H Wu, Y Jiang, X Lu, and D Pang. Phosphoglycerate kinase-1 is a predictor of poor survival and a novel prognostic biomarker of chemoresistance to paclitaxel treatment in breast cancer. *British Journal of Cancer*, 112(8):1332–1339, April 2015.
- [2] X Yu and S Li. Non-metabolic functions of glycolytic enzymes in tumorigenesis. *Oncogene*, 36(19):2629–2636, May 2017.