Pre-treatment energy status of primary rat tumours as the best predictor of response to 5-fluorouracil chemotherapy: a magnetic resonance spectroscopy study in vivo

Titre	Pre-treatment energy status of primary rat tumours as the best predictor of response to 5-fluorouracil chemotherapy: a magnetic resonance spectroscopy study in vivo
Type de publication	Article de revue
Auteur	Lemaire, Laurent [1], McSheehy, Paul [2], Griffiths, John R [3]
Editeur	Springer Verlag
Type	Article scientifique dans une revue à comité de lecture
Année	1998
Langue	Anglais
Pagination	201-209
Volume	42
Section	3
Titre de la revue	Cancer Chemotherapy and Pharmacology
ISSN	0344-5704
Mots-clés	19F/31P [4], 5-Fluorouracil [5], NMR spectroscopy [6], Primary tumours [7]

Résumé en anglais	Purpose: Fluorine-19 magnetic resonance spectroscopy (F-MRS) studies of the pharmacokinetics of the anticancer drug 5-fluorouracil (FU) in patients at several clinical centres have shown that increased tumour retention of FU is associated with patient response. The mechanism of this increased tumour retention (FU trapping) is unknown. We used a pre-clinical model to investigate whether other MRS-measurable parameters would correlate with the response to FU treatment and, thus, help elucidate the mechanism(s) involved in FU trapping. Methods: MRS spectra were obtained using a double-tuned (P-31/F-19) surface coil from 29 N-methyl-N-nitrosourea-induced primary rat rumours. P-31-MRS spectra were acquired immediately prior to and at 2.5 h post-treatment with a bolus i.p. injection of FU (100 mg/kg); F-19-MRS spectra were acquired during the intervening 2.5-h period for measurement of the tumour uptake and retention of FU and of its metabolism to the cytotoxic fluoronucleotides (FNuct). From these data, four parameters were measured: tumour pH and energy status (NTP/Pi) before treatment, total FU retention, and FU anabolism to FNuct (expressed as micromoles per gram per 2.5 h). In addition, tumour response was determined at 7 days post-treatment by measurement of the percentage of change in tumour weight and was classified according to standard oncological criteria as follows: progressive (P) for a 225% increase, remissive (R) for a greater than or equal to 50% decrease or stable (S) for values lying between these two. Results: Analysis of variance (ANOVA) for statistical assessment revealed that groups P, S and R were not distinguishable using the MRS parameters; although when S and R were combined as one group of non-progressive disease (NPD; n = 24), both the NTP/Pi ratio and the total FNuct formed were significantly greater (P = 0.03) than those observed in the P group (Iz = 5). Considering all 29 tumours, linear regression showed that there were positive significant correlations between the NTP/Pi ratio and (a) the percentage of response (P = 0.04), (b) the pre-treatment pH (P = 0.002) and (c) FU retention (P = 0.02), but not FNuct formation(P = 0.66). Unlike results reported in the clinic, the percentage of response and FU retention were neither significantly correlated (P = 0.22) nor associated when groups P and NPD were compared (P = 0.27, Fischer's exact test). FNuct, however, was significantly associated with response, as was the NTP/Pi ratio (P less than or equal to 0.02). Combination of FNuct with the NTP/Pi ratio increased the significance of the association with response (P = 0.003, Fischer's exact test). Conclusions: Our results indicate that in this particular model the pretreatment tumour NTP/Pi ratio was the best predictor of response to a bolus injection of FU, rather than FNuct formation or FU retention. An elevated NTP/Pi ratio could reflect a well-vascularised tumour with an improved capacity for energy-dependent FU uptake and metabolism to FNuct, suggesting that further investigation of this parameter could be an important line of research, which may aid the identification of tumours likely to be sensitive to FU chemotherapy in the clinic.
URL de la notice	http://okina.univ-angers.fr/publications/ua5688 [8]
DOI	10.1007/s002800050806 [9]

Liens

[1] http://okina.univ-angers.fr/l.lemaire/publications
[2] http://okina.univ-angers.fr/publications?f[author]=9533
[3] http://okina.univ-angers.fr/publications?f[author]=9532
[4] http://okina.univ-angers.fr/publications?f[keyword]=10269
[5] http://okina.univ-angers.fr/publications?f[keyword]=8396
[6] http://okina.univ-angers.fr/publications?f[keyword]=10270
[7] http://okina.univ-angers.fr/publications?f[keyword]=10271
[8] http://okina.univ-angers.fr/publications/ua5688

[9] http://dx.doi.org/10.1007/s002800050806