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| Nutrients Editorial Office |
| Re. Submission of manuscript for consideration |

Dear Prof. Dr. Maria Luz Fernandez and Prof. Dr. Lluis Serra-Majem,

We are pleased to submit our manuscript entitled “Substitution of red meat with legumes and risk of primary liver cancer in UK Biobank participants: a prospective cohort study” for consideration by *Nutrients* as an original article. This new submission is by invitation with a 100% discount.

Research on the general health benefits of including legumes in the diet and the adverse effects of red meat are substantial. However, the association of these foods with liver cancer incidence is understudied and the current literature fails to reflect that a higher intake of one food is at the expense of another. We investigated the association of replacing 15 g/day of total, unprocessed, and processed red meat with legumes and risk of developing primary liver cancer. To our best knowledge, this is the first study on food substitutions investigating and risk of both hepatocellular carcinoma and intrahepatic cholangiocarcinoma, the two main types of primary liver cancer.

We used the UK Biobank cohort including middle-aged men and women with at least two 24-hour dietary recalls (N = 126,744; 173 cases over 11.1 years). Contrary to our hypotheses, we found no association between replacing red meat with legumes and liver cancer risk after adjusting for multiple potential confounders (total red meat HR: 1.02, 95% CI: 0.96-1.08; unprocessed red meat HR: 1.00, 95% CI: 0.94-1.06; processed red meat HR: 1.09, 95% CI: 0.99-1.21). Nevertheless, substituting animal-based foods with plant-based are important if we are to lower the climate impacts of our diets. We believe that the readers of Nutrients will find our study relevant as it contributes knowledge on the impact of food substitutions on human health and elaborates on a practical method for assessing food substitution associations.

We confirm that neither the manuscript nor any parts of its content are currently under consideration for publication with or published in another journal. All authors have approved the manuscript and agree with its submission to *Nutrients*.

Kind regards

Diagram

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