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### **The impact of socioeconomic status on the molecular epidemiology of esophageal cancer**

Esophageal cancer (EC) is one of the ten most common causes of death by cancer worldwide. Its late diagnosis together with the inefficient treatment are the main factors associated with the poor prognosis. Therefore, prevention and early diagnosis are key aspects of EC control. EC includes two main histological types, adenocarcinoma (EADC) and squamous cell carcinoma (ESCC), which differ in terms of affected populations, associated risk factors, and molecular mechanisms. In Brazil, as well as in other low-and-middle income countries, ESCC accounts for more than 80% of EC cases. Its development is associated with a life-long exposure to alcohol and tobacco in Brazilians, but in other populations other risk factors, such as betel quid and hot beverages, are more common.

Despite these differences, a common characteristic of the populations affected by ESCC is the low socioeconomic status (SES). SES is a complex trait and different variables have been used to capture SES in epidemiological studies, such as education levels, household income, and wealth scores. However, other aspects of SES cannot be disregarded when considering its association with ESCC development. Diet and changes in the esophageal microbiome have already been associated with ESCC risk. Based on this, IARC is well-placed to help guide us on the development of projects focusing on the impact of SES on ESCC development, with specific attention placed on nutritional aspects, metabolism, and microbiome. This knowledge, together with the experience of my group on molecular alterations, may shed light on the molecular mechanisms behind the association between low SES and ESCC.

Within this collaboration, we initially intend to explore differences in ESCC microbiome according to SES, and correlate them with DNA methylation patterns, response to therapy, and overall survival. Then, we plan to extend the analyses to include metabolome and nutritional status. Therefore, the proposed collaborative study will not only gather data on the molecular mechanisms through which low SES contributes to ESCC development, but also contribute to the development of future molecular epidemiology studies in the Brazilian National Cancer Institute through the dissemination of the knowledge acquired.