Reply to "Dietary glucosinolates and risk of type 2 diabetes in 3 prospective cohort studies"

Dear Editor:

We read the article entitled "Dietary glucosinolates and risk of type 2 diabetes in 3 prospective cohort studies" (1) on the association of *Brassica* vegetable consumption and the incidence of type 2 diabetes (T2D) with great interest. In this study the authors stated that they wanted to test the hypothesis that the activation of the nuclear factor E2-related factor (Nrf2) pathway plays an important role preventing T2D and reducing insulin resistance. Since sulforaphane is an activator of Nrf2, their hypothesis was that it may reduce T2D incidence (2). According to the results of their study, the author stated: "participants in the highest quintile of total glucosinolate intake had a 19% higher risk (95% CI: 13%, 25%; *P*-trend $<$ 0.001) of T2D than did those in the lowest quintile" (2).

However, we think that the study has major flaws in testing the initial hypothesis. Both the food frequency questionnaire and the databases that were used for the calculation of the intake of glucosinolates (GLs) did not take into account the effect of processing and preparation of the vegetables, which are known to have a major impact on the retention of GLs (3, 4). Moreover, the authors have based the calculation on the total GL intake, whereas the bioactive compound investigated should have been sulforaphane or its precursor GL, glucoraphanin, that is mainly present in broccoli and red cabbage. Instead, the authors have considered all the *Brassica* and all the GLs, rather than the real bioactive isothiocyanates (ITCs), without discrimination of which type.

The authors based the GL intake on a publication (5) in which a database on GL concentrations in different vegetables was developed by taking GL concentration values from several published research studies. However, studies have clearly shown major difficulties in estimating the GL content in the final plate (6), and even more complications in estimating the formation of ITCs.

Factors such as the activity of the GL-catalytic endogenous enzyme (myrosinase) and its cofactors, the inactivation of the specifier proteins that would lead to higher formation of nitriles rather than ITCs, and the pH, all affect the formation of ITCs—e.g., cooking can drastically reduce the potential formation of ITCs by inactivating the endogenous myrosinase, and in some cases also reduce the GL content (4, 7). Therefore, since *Brassica* vegetables are often consumed after cooking, a very low formation of ITCs will occur. During digestion only a small part of GL may be hydrolyzed by the intestinal microbiota to form ITCs, and the extent of such hydrolysis can be very different among individuals and meals (8, 9). Therefore, the type of cultivars, the cultivation conditions, the storage conditions, the preparation methods, the domestic handling and cooking, and the microbiota profile dramatically affect the concentration of the GLs, of the endogenous enzyme, and the formation of ITCs.

We think that the inclusion of all GLs (upon which the calculation was based) and the very high variability of the bioactive ITCs intake have seriously compromised the reliability of the study conducted and therefore its conclusions are highly debatable.

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Note: The authors of the original article chose not to submit a reply.

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Abbreviations used: GL, glucosinolate; ITC, isothiocyanates; T2D, type 2 diabetes.

