Reaction of EU-LIFE:
Cancer Mission work programme 2021-22

On 15 December 2021 the European Commission published the Work Programme 2021-2022 for the Missions, including the Work Programme for the Cancer Mission. As an alliance of life science institutes we are very committed to solving the cancer problem and are therefore very much interested in the Work Programme. We applaud the European Commission and the Cancer Mission Board for their first Work Programme, but we also have several concerns. These concerns are similar to the recommendations we published in September 2020 for drafting the Cancer Mission Work Programme (link).

Our most serious concern is that **unrealistic expectations** are formulated in the expected outcome section of each call; unrealistic with respect to scope, expected outcomes and involvement of (a too broad) range of stakeholders. We are afraid that these very broadly formulated outcomes will deter excellent scientists to participate in these call as they feel they cannot life up to the formulated expectations. It might also lead to disappointment among policymakers and the general public. It should be noted that the ambition to develop a pan-European platform consolidating clinical data would indeed benefit translational cancer research, but requires substantial reform and harmonization of current laws and policies. We realize that the budgets are substantial and that serious impact should be generated, but the currently formulated expectations seem unrealistic.

Furthermore, we consider there is **not sufficient weight to higher risk, bottom-up collaborative approaches** to achieve the intended long-term impact of the Cancer Mission. It will be essential that the next work programmes re-address the balance between high risk and closer to the user approaches. We repeat our previous concern that some of the proposed actions in this Cancer Mission Work Programme should not be supported through the Horizon Europe programme (and budget), since they are not on innovation or research but more focussed on organisation of stakeholders. This should be carefully avoided in all work programmes of the Cancer Mission.

We are glad to see that some of the topics that we proposed in our 2020 recommendations have been incorporated in the current Cancer Mission Work Programme (e.g. Quality of Life research and early detection). We hope to see the other topics, equally important, incorporated in the next Cancer Mission Work Programmes.

CANCER MISSION WORK PROGRAM 2021-2**:**
https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/wp-call/2021-2022/wp-12-missions_horizon-2021-2022_en.pdf

EU-LIFE Recommendations to Cancer mission programme here:
https://eu-life.eu/sites/default/files/2020-09/EULIFE_Recomendations_CancerMission_28SEP20.pdf

Recapitulation of previously given recommendations

1. Our most serious concern is that the emphasis of the work programme is entirely on data gathering, identification of discriminating features for treatment and attempts to apply this for more effective treatments. Whilst these efforts merit funding, they will only be effective in the long term if they are coupled with sufficient efforts to explain the molecular basis for discriminating features.
2. Likewise, we consider there is not sufficient weight to higher risk, bottom-up approaches to achieve the intended long-term impact of the Cancer mission. It will be essential that the next work programmes re-address the balance between collaborative high risk projects

to unravel the molecular mechanisms of various kind of cancer and more translational approaches. Furthermore, research is needed on cancers for which there is yet no treatment available; the current focus on improving already available treatments will not address the full range of challenges we face currently.

3. We also reinforce our previous concern that some of the proposed actions in the cancer mission are not directly related to innovation or research. While we recommend that some of these actions, such as those targeted to supporting cancer patient quality of life, could be retained but with much lower budget compared to those on innovation and research actions. Also actions mainly aimed at industrial collaborations should not be supported through the Horizon Europe programme (and budget).

4. We welcome the fact that the budget is substantial and allows for several large projects. However, we are concerned about unrealistic expectations formulated for each project regarding scope, expected outcomes and involvement of (a too broad) range of stakeholders in each.

5. We support transversal emphasis not only on genetic determinants but also on socioeconomic status, behavioural, lifestyle and environmental factors.

6. We support emphasis on inclusiveness through the transversal request for addressing social, cultural, sex and gender aspects as well as inequalities in all proposals.

7. As we have recommended during the consultation stage, we welcome the efforts in investing in research on the quality-of-life studies, since this has been neglected in the past.

Specific Recommendations for the UNCAN.eu project

We welcome the initiative to bring together as much data as possible to address timely and pressing scientific and medical challenges in the field of cancer. We would like to highlight the following challenges that urgently need answers.

In general: **Emphasis on understanding underlying molecular and cellular mechanisms of disease and exploiting them towards treatment, especially precision oncology, including:**

- **Cancer cell dormancy** and its implications in cancer recurrence/relapse and metastasis.

- **Tumour genomic heterogeneity and tumour evolution**. This includes: visualisation of early lesions; identification of progenitor cells and non-mutant surrounding cells that importantly contribute to cancer development; evolution and therapy resistance specific early biomarkers; validation of new early biomarkers in mouse models & clinical samples. To this end, we recommend that specific calls would include **exploitation of novel technologies** e.g. single cell RNA sequencing and patient-derived 3D organoid models in “Understand” and “Treatment” actions.

- Cancer is a multifactorial disease that depends on alterations occurring at the cellular level that **influence and are influenced by the organism,** hence animal models are still indispensable in order to be able to establish causality.

- Discover novel vulnerabilities of cancer by approaching cancer as a whole organ disease by focusing on **the bidirectional interplay between cancer cells and the Tumour MicroEnvironment (TME)**.

- Exploring crosstalk with the **Tumour MacroEnvironment (TMA)** such as the physiology of the host organ and organism.

- Investigating how cancer cells affect the function of **distant organs** and how **lifestyle factors** (such as diet) shape tumour evolution and therapy efficacy.

- Understanding how the **tumour ecosystem** reprograms cancer cells towards increased survival, proliferation, migration and evasion of the effects of therapy.

- **Cancer immunotherapy** - more research for enhancing the benefits of immunotherapy, eg modifying immune susceptibility of tumours

- **Environment and lifestyle related risks:** how will lifestyle, and sociodemographic factors be accounted for and which part of the program will be "extended to other diseases".

- Identifying **novel "actionable" genomic targets** independent of histology of origin in line with a pathway-driven therapeutic approach.

- Longitudinal follow-up studies of **pre-malignant cases** to recognise the role of serial genetic abnormalities in association with environmental factors, lifestyle etc. Such studies may be supported by existing consortia of pre-malignant patients with available patient data and biobanks. Special focus on incurable cancers or those with bad prognosis.

- Increase and support **drug repurposing for cancer treatments**: There are many good (targeted) drugs available for disease A, and it remains difficult to get that drug available for, for example, a rare cancer. Within the Cancer mission, pharma should be stimulated to follow this approach, which could fit into the section 'personalised medicine': for example develop ways to stimulate repurposing of approved drugs for rare cancers.

- Specific programs that include the exploitation of **machine learning and artificial intelligence** for predicting the response to anticancer therapies.

Barcelona, February 2022