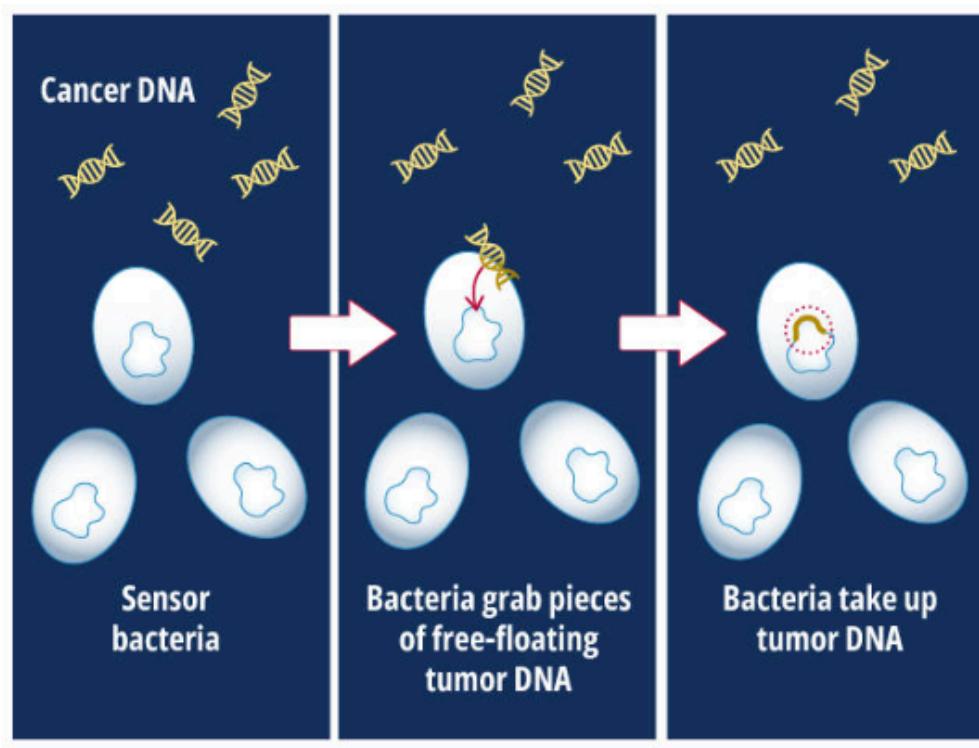


1. First, describe a biological engineering application or tool you want to develop and why.

Bio-sensors/Living sensors is not a new concept, till date it has been used for several purposes i.e used to detect metals in water, metabolites in bioreactors, pathogens in food, and plant stress signals in agriculture. But what if they could sense tumors in body and help with cancer detection? My interest lies in cancer biology and making use of syn bio in combating this disease is something I want to do. Designing and engineering a bacteria that could sense tumor specific signals in the body and produce a response in the form of fluorescence or a secreted biomarker. This will not only help with early cancer detection and improve treatment outcomes but also could help complement existing diagnostics and reduce invasive procedures by detecting specific metabolites or surface markers associated with tumors.



Credit: National Cancer Institute

2. Next, describe one or more governance/policy goals related to ensuring that this application or tool contributes to an “ethical” future, like ensuring non-malfeasance (preventing harm). Break big goals down into two or more specific sub-goals

Keeping COVID as an example of an intended or unintended release or spread of genetically engineered or naturally mutant variants that took the whole world by storm and had adverse after effects. So the ultimate goal would be to make sure that the engineered tumor sensing bacteria is developed and used in an ethical way, which prioritizes safety, environmental stewardship, and social responsibility. In order to achieve this goal, the risk of unintended

pathogenicity, horizontal gene transfer and adverse host immune responses should be minimized by keeping the principle of non-malifrance in mind. Side by side for environmental safeguards necessary actions that would prevent persistence, dissemination, ecological disruption needs to be taken, to restrict the engineered bacteria to the intended use only. Furthermore, the ethical use of this technology means to make sure everyone has access to the applications of this technology so that the benefits are equally distributed among the people.

3. Next, describe at least three different potential governance “actions” by considering the four aspects below (Purpose, Design, Assumptions, Risks of Failure & “Success”).

Governance Actions

1. Bio-safety

Engineered microorganisms are tested for basic lab safety, but they need to be tested for genetic kill-switches and immunogenicity and containment before making them accessible to humans. The protocols for these tests must be standardized by the regulators (FDA, EMA). These studies must be funded by Academic labs and companies. Without approval clinical trials cannot be done. Let's suppose the lab test successfully and reliably predict the behaviour of the bacteria in the body and kill switches functioned properly. In case of failure the bacteria causes infections and survives outside the body and in case of success the bacteria was a success and it reduced patient risk but due to regulatory burden the research could be slowed down.

2. Incentives for fair access and ethical use: To make the technology accessible to everyone, it needs to be commercialized but commercialization prioritizes profit. For fair access and ethical use, we can fund incentives and issue ethical guidelines to be followed by the labs and companies. Funding agencies should only approve the grants that mention a plan for fair access. And the Universities and companies can provide training for responsible research and innovation. Supposedly financial incentives could change the attitude and make them follow the guidelines. Companies may skip the incentives limiting the impact if profit remains the main goal.

3. Environmental containment & monitoring

Different labs follow different containment protocols. Standardized protocols should be established, gut simulator models should be used for testing and routine environmental monitoring should be performed in order to prevent accidental release and minimize environmental risk. The Regulatory bodies, Biotechnological companies and the academic laboratories should implement rules for containment, monitoring and reporting. Labs following the standardized protocols might be on a safer side and the monitoring technology could help detect the accidental releases at its earliest. The risk associated with this could be human errors or system failure, and could provide false security if the protocols are not updated. The success could provide environmental safety but to make sure it works would require extra training and cost.

4. Next, score (from 1-3 with, 1 as the best, or n/a) each of your governance actions against your rubric of policy goals. The following is one framework but feel free to make your own:

Does the option:	Option 1	Option 2	Option 3
Enhance Biosecurity			
• By preventing incidents	1	2	2
• By helping respond	1	2	2
Foster Lab Safety			
• By preventing incident	1	2	2
• By helping respond	1	2	2
Protect the environment			
• By preventing incidents	2	2	1
• By helping respond	2	2	1
Other considerations			
• Minimizing costs and burdens to stakeholders	3	1	2
• Feasibility?	2	1	2
• Not impede research	3	1	2
• Promote constructive applications	1	1	2

5.Last, drawing upon this scoring, describe which governance option, or combination of options, you would prioritize, and why. Outline any trade-offs you considered as well as assumptions and uncertainties.

I would prioritize option 1 in combination with option 2 based on the scoring, the combination of both can give maximum safety to the humans and the environment, as these are priority when it comes to ethical concerns. Though option 2 is also valuable but as serves a secondary, because it can be promoted with the help of incentives and training programs. Although prioritizing the combination of these options would slow down the research as regulatory and containment can increase the cost and time for the laboratories and the companies and also standardized training requires equipment and staff training. Assuming that Genetic-switch works properly and can predict the behaviour of the bacteria accurately. Laboratories and companies are adhering to the safety, containment and monitoring protocols. And no ecological disaster occurs if the bacteria are accidentally released into the environment.

References

- Panteli JT, Forbes NS. Engineered bacteria detect spatial profiles in glucose concentration within solid tumor cell masses. *Biotechnol Bioeng*. 2016 Nov;113(11):2474-84. doi: 10.1002/bit.26006. Epub 2016 Sep 20. PMID: 27159665; PMCID: PMC5037000.
- Zúñiga A, Camacho M, Chang HJ, Fristot E, Mayonove P, Hani EH, Bonnet J. Engineered L-Lactate Responding Promoter System Operating in Glucose-Rich and Anoxic Environments. *ACS Synth Biol*. 2021 Dec 17;10(12):3527-3536. doi: 10.1021/acssynbio.1c00456. Epub 2021 Dec 1. PMID: 34851606; PMCID: PMC8689689.
- Chien T, Harimoto T, Kepecs B, Gray K, Coker C, Hou N, Pu K, Azad T, Nolasco A, Pavlicova M, Danino T. Enhancing the tropism of bacteria via genetically programmed biosensors. *Nat Biomed Eng*. 2022 Jan;6(1):94-104. doi: 10.1038/s41551-021-00772-3. Epub 2021 Jul 29. PMID: 34326488; PMCID: PMC8956018.
- <https://www.cancer.gov/news-events/cancer-currents-blog/2023/engineered-bacteria-detect-cancer>
- Ma X, Liang X, Li Y, Feng Q, Cheng K, Ma N, Zhu F, Guo X, Yue Y, Liu G, Zhang T, Liang J, Ren L, Zhao X, Nie G. Modular-designed engineered bacteria for precision tumor immunotherapy via spatiotemporal manipulation by magnetic field. *Nat Commun*. 2023 Mar 23;14(1):1606. doi: 10.1038/s41467-023-37225-1. Erratum in: *Nat Commun*. 2023 Jul 10;14(1):4067. doi: 10.1038/s41467-023-39906-3. PMID: 36959204; PMCID: PMC10036336.