Pancreatic ductal adenocarcinoma (PDAC) is one of the top 10 leading causes of cancer death worldwide. Although over 10% of patients may be resectable at presentation in specialized centers, median survival is only 12-18 months with less than 10-20% of resected patients surviving beyond five years. This is because the symptoms and signs of pancreatic cancer are highly nonspecific, causing patients to be diagnosed at an advanced stage.

Abstract

**Objectives:** This project examines new effective target nanoparticles molecules for Pancreatic Cancer Therapy (PCT). Metal-organic frameworks (MOFs) are hybrid materials formed by metals ions and bridging ligands. Because metals and ligands can be combined in an almost infinite number of ways, with each unique combination having correspondingly unique properties, physicochemical properties of MOFs can be tuned for specific applications. For this project, MOFs may be used as delivery vehicles for imaging agents, drug molecules, and electron donating groups, possessing advantages over existing nanocarriers.

**Methods:** In this paper, an open-source molecular editing program with an auto-optimization feature that is able to determine the theoretical values of a structure’s atomic properties, to model MOFs. The program enables users to build virtually any molecule and will find its optimal geometry based on energy minimization calculations.

**Data and Conclusion:** Twenty porous metal-organic frameworks were chosen to undergo bio-computational analysis in the treatment of tumor cell. Zn$_4$(O$_2$C$_2$)$_8$ compound had an optimization energy of 325 kJ/mol and thus was the thermodynamically most stable compound. Zn$_4$(O$_2$C$_2$)$_8$ was the computationally most stable, but least functional (smallest surface area) one. MOF-200 was best taken after accounting in stability and functionality.

**Introduction**

Pancreatic ductal adenocarcinoma (PDAC) is one of the top 10 leading causes of cancer death worldwide. Although over 10% of patients may be resectable at presentation in specialized centers, median survival is only 12-18 months with less than 10-20% of resected patients surviving beyond five years. This is because the symptoms and signs of pancreatic cancer are highly nonspecific, causing patients to be diagnosed at an advanced stage.

**Model Parts**

**Linker+Joint**

**Nanoparticles**

- Electron properties of functionalized MOFs will be used as effective contrast agents.
- High porosity of MOFs can allow for efficient drug delivery.
- Electron donating groups can be attached to MOFs which will mitigate the effects of ROS.

**MOF Structures**

- High porosity and functionalized groups to yield a structure with high porosity and long life cycles.

MOFs are capable of combining desirable features of both carbon and metal-oxide materials to yield a structure with high porosity and long life cycles.

**Test Structural Versatility**

- MOFs are capable of combining desirable features of both carbon and metal-oxide materials to yield a structure with high porosity and long life cycles.

**Combining the Parts**

- Combining the Parts
- Example: Simulation of MOF-5 with a molecular weight of 3,518.6 kDa and optimized energy of 6,316 kJ/mol

**Optimized Energy Measurement & Analysis**

**Materials**

- 20 compounds were chosen for their various structure types, organic ligands, and general geometry to be used in computer simulations.
- 8 to 15 possible linkers that may be used in between the joints.

**Stereochecal and Thermodynamic Analysis of the Metal-Organic Frameworks (MOFs) for the Pancreatic Cancer Therapy (PCT)**

**Discussion**

- Following a thorough analysis of twenty representative porous metal-organic frameworks, we found that Zn$_4$(O$_2$C$_2$)$_8$ was the thermodynamically most stable compound as a joint. For linkers, Zn$_4$(O$_2$C$_2$)$_8$ was the computationally most stable, but least functional (smallest surface area) one. Thus, MOF-200 was the best linker after taking into account stability and functionality.

**Conclusion**

- Twenty porous metal-organic frameworks were targeted for their representation of a wide variety of structure types, metrics, sizes and functionalities of pores to undergo computational analysis by studying their nanocarboxylate form, performance, and properties as PCT. Their nature as easily synthesized compounds and bioavailability alongside their wide variety of potential applications, including delivery vehicles for contrast agents, drug molecules, and electron donating functional groups renders them as strong candidates for a new generation of cancer-treatment.

- Following our computational analysis of the chosen MOFs, it is significant that the energy profiles of these MOFs change differently and follow the general behavior expected in VSPPR theory. Additionally, it is found that as we increase functionality, the optimization energy increases correspondingly - meaning that more effort/energy is required in order to stabilize the compound. Optimally, we do not want high complexity, which would entail increased porosity and thus function, but also stability and efficiency. However, there is always a trade-off between stability and functionality.

- Ultimately, it is found that Zn$_4$(O$_2$C$_2$)$_8$ with (3-MOF-200) as linkers would be the optimal MOF under the given conditions.

- Future work may take a few directions.
  - One is the continued investigation of a variety of factors such as reactivity/conductivity and electrostatic potential of MOFs for optimization.
  - It may be wise to focus on deciphering the specific impacts of various MOF structures on the optimization energy.
  - It can also look out translating such optimized structures into a reality and utilizing them in actual clinical trials.