

Metal Organic Frameworks – A New Drug Delivery Approach to Improving the Outcome of Treatment of the Childhood Cancer, Neuroblastoma

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Introduction

- Neuroblastoma (NB) is responsible for 15% of all childhood cancer-related deaths.
- Treatment outcome remains poor with current treatments like chemotherapy, radiotherapy, and immunotherapy.
- Recent evidence suggests that compounds from the fungi, *Aspergillus fumigatus*, have anticancer properties, but targeted delivery of these compounds remains a challenge.
- Metal organic frameworks (MOFs), an exciting development in the field of material chemistry and engineering possess certain characteristics that makes them ideal candidates for targeting these fungal derived compounds to neuroblastoma cells.

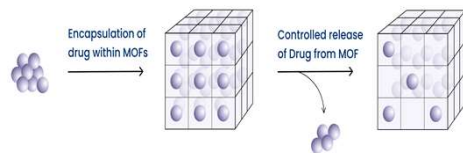
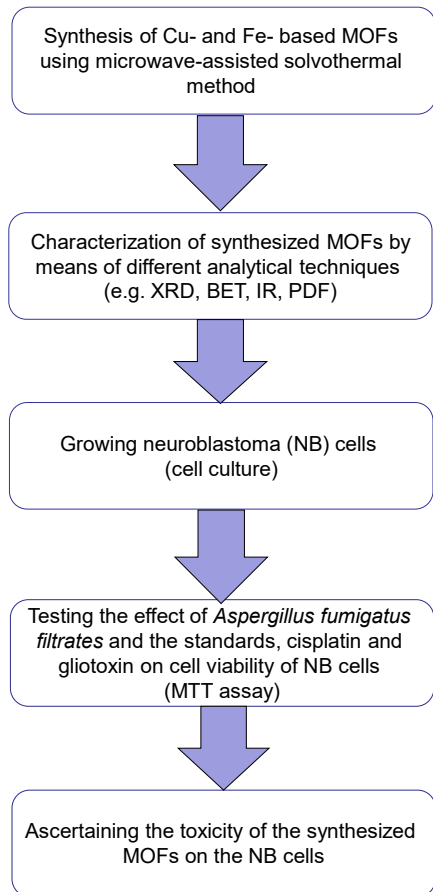


Figure 1: Schematic of loading of drug within a MOF and controlled release of the drug from within the framework (Adapted from Keskin & Kizilel, 2011).

- Our study seeks to identify compound(s) with anticancer properties from two different *Aspergillus fumigatus* filtrates (AF293 and CEA10), encapsulate these compounds within MOFs synthesized in our lab and target these MOF-drug systems to neuroblastoma cells.

Methods



Results

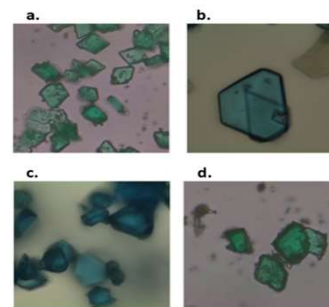


Figure 2: Optical micrographs of crystals of some Cu-based MOFs synthesized in our lab under different synthesis conditions. **a.** Crystals of **MOF5CuAIPA130** synthesized in DMF for 5 minutes at 130°C. **b and c.** Crystals of **MOF30CuAIPA130** synthesized in water/ethanol for 30 minutes at 130°C. **d.** Crystals of **MOF30CuAIPA130** synthesized in DMF for 30 minutes at 130°C.

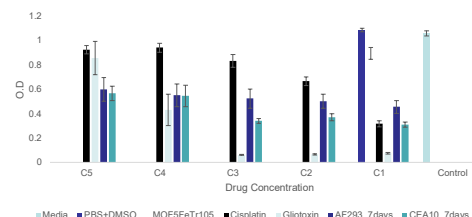


Figure 3: Cell viability of SHSY-5Y cells. NB cells were exposed to control media, media containing different concentrations of PBS/DMSO, MOF5FeTr105, cisplatin, gliotoxin, AF293 and CEA10, respectively, for 24 hours, and cell viability assessed using MTT assay. Data is presented as mean \pm SEM, $n = 6$ per group.

Conclusions

- In our lab, MOFs can be successfully synthesized at short times using the microwave-assisted solvothermal method.
- These MOFs are non-toxic against neuroblastoma cells.
- The filtrates from the two *Aspergillus fumigatus* species (AF293 and CEA10) showed anticancer activity against neuroblastoma cells.

These interesting results have provided the premise for the future work that would be carried out in our lab, and this will be directed towards the following:

- Optimizing the synthesized MOFs for drug delivery.
- Identifying which compound(s) present in the *Aspergillus fumigatus* filtrates is responsible for killing the NB cells.
- Encapsulating this/these compound(s) within the MOFs and targeting them to neuroblastoma cells.

References

- [1] Zhang, Y., Huang, D., Zhang, W., Tang, S., Han, T., Zhu, X., Liu, A., & Zhi, T. (2016). Clinical characteristics of infant neuroblastoma and a summary of treatment outcome. *Oncology Letters*, 12(6), 5356–5362
- [2] Keskin, S., & Kizilel, S. Biomedical Applications of Metal Organic Frameworks. *Ind. Eng. Chem. Res* 2012, 50, 1799–1812. <https://doi.org/10.1021/ie101312k>