EVEN LOW HANGING FRUIT CAN BE DIFFICULT TO REACH
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1. no conflicts of interest
2. i will be discussing off label use of drugs.
3. no herbal, nutitional supplements, or non-FDA, non-EMA drugs.
eleven core principles of repurposing drugs for cancer treatment with three recent examples.
repurposing is really unrepurposing.
recognize attributes -
match drug attribute to a cancer
physiological attribute.
constraints:
cheap, well understood, low risk.
DIYers. no profit. regulatory difficulties.
peer criticism, institutional restrictions,
legal fears, poor understanding of cancer physiology & drug action
Nile distributary problem. example:

anlotinib - multi-target TKI.

targets VEGF receptor, FGF receptor, PDGF receptor, and stem cell factor receptor (c-Kit) - 3.3 month PFS was called an “an effective regimen” in NSCLC.
Nile distributary Problem.

Cancers (Basel). 2019;11(7). pii: E892

horizontal intercellular transfer of resistance, mitochondrial & extrachromosomal circular DNA
cancers have no achilles’ heel.

[ like all well engineered machines ]

cf. basal cell carcinoma
shaping operation

1 2 3 4 5

decisive operation

6 7 8 9 10 11

clean room,
sterile instruments,
food & laundry service,
anesthesia,
blood bank,
administration, finance, accounting

resection
(irradiation)
in cancer treatment, repurposed drugs tend to be shaping operations
a] 1 thru 5 above imply need for polypharmacy.
b] meds must be coordinated.  
   cf. 3 locks problem.
c] celecoxib, chloroquine, disulfiram, metformin, statin, valproate failures…..
if one tries to hold onto everything, one ends by holding onto nothing.
[ overavoid SE, gross underdosing i.a. ]
chess aphorism:
all moves create strengths and weaknesses

[our interventions have pro tumor growth aspects plus anti-tumor growth aspects]
cancers are not passive recipients of our interventions. Every growth retarding intervention engages compensatory growth restoring reaction.
surgery, irradiation, and cytotoxic chemotherapies deliver a get-up-and-go signal. Cancers exhibit accelerating aggressiveness over time.
mechanism based
or
empirically based
# 5-ALA CAALA Regimen

<table>
<thead>
<tr>
<th>Drug</th>
<th>Marketed</th>
<th>Function in CAALA</th>
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<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>ABX</td>
<td>Impair mitochondria</td>
</tr>
<tr>
<td>Deferiprone</td>
<td>Fe reduction</td>
<td>Less PpIX to heme</td>
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<tr>
<td>5-Fluorouracil</td>
<td>Cytotoxin</td>
<td>Mitochondria damage</td>
</tr>
<tr>
<td>Febuxostat</td>
<td>Uricosuric</td>
<td>Inhibit 5-ALA efflux</td>
</tr>
</tbody>
</table>

1. Methylene blue inhibits NLRP3 inflammasome function.

2. NLRP3 essential in MDS marrow destruction

Kast RE. Inhibiting the NLRP3 Inflammasome With Methylene Blue as Treatment Adjunct in Myelodysplasia. Front Oncol. 2018;8:280.
Principal investigator -

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nine repurposed general medicine drugs to augment temozolomide in recurrent glioblastoma
1. aprepitant…….80 mg x 1 [ lorazepam
2. auranofin........3 mg x 2 hydromorphone
3. captopril.........50 mg x 2 loperamide
4. celecoxib........400 mg x 2 V-8, miso, broth
5. disulfiram.......250 mg x 2
6. itraconazole.....200 mg x 2
7. minocycline.....100 mg x 2
8. ritonavir.........400 mg x 2
9. sertraline........100 mg x 2
10. temozolomide...20 mg/m² BSA x 2
good tolerability
PFS12 = 50%
PFS18 = 40%
no drug related withdrawals
but ensemble not cheap
grade 1 or 2 fatigue was common
F-22A = $68,000 / hour

F-16 = $25,500 / hour

F-35 = $30,000 / hour

UK’s Merlin Mk 3, £42,000 / hour
https://clue.io/repurposing
1. **CUSP9v3** for GB
2. **ADZT** apramilast, dapsone, zonisamide, telmisartan to augment bevacizumab
3. **5aai** 5-ALA augmented irradiation for DIPG
4. **MB** methylene blue for myelodysplasia
5. **ABC7** for breast cancer capcitabine, quetiapine, pirfenidone, rifabutin, metformin, propranolol, agomelatine, ribavirin
6. **CAALA** cipro, 5-FU, febuxostat, deferiprone to augment 5-ALA
7. **EIS** itraconazole, metformin, naproxen, pirfenidone, quetiapine, rifampin for GB
8. **DFR** dapsone, fenofibrate, ribavirin to lower G-CSF function in GB
9. **MTZ** minocycline, telmisartan, zolidronic acid in GB
10. **PMC**plerixafor, mirtazapine, clotrimazole for GB
even low hanging fruit can be difficult to reach