**Literature Review: Contemporary and Historical Treatments of Cancer**

Author: Christian Roopnarinesingh  
Major: Integrative Biology  
Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

**Key Words:**

Transcription factors, drug resistance determinants, polychemotherapy, tumor heterogeneity

**This review will inspect two journals that feature divergent causes and treatments of cancer. The journals approach determinants of drug resistance in cancer, which includes tumor burden, tumor heterogeneity, physical barriers, and tumor microenvironments. Additionally, the journals describe indicators and causes of cancer growth, such as the deregulation of MYC transcription factors. Both journals go in depth about potential – and empirical – treatments to cancers, that depend on the type of cancer and tumor.**

**Introduction**

In this introduction, the two journals will be separated to help distinguish what they focus on, so the key concepts for both can be understood.

**A View On Drug Resistance In Cancer:**

Drug resistance in cancer has proven to be a difficult blockade to surpass. Tumors often go into states of remission, only to develop resistance against the chosen therapies. The main purpose of this journal is to enumerate the determinants of drug resistance in cancer. The authors take a reductionist approach to the variables of drug resistance by individualizing them, which was done to increase targeted accuracy of treatments (Allen-Petersen et al. 2019). Targeted therapies are currently a strong focus in oncology to combat drug resistance because polychemotherapy and other forms of therapy that indiscriminately combat cancer were promising at first, but have plateaued in their ability to consistency result in successful treatment. The four selections of drug resistance are tumor burden/growth kinetics, tumor heterogeneity, physical barriers. And tumor microenvironments. Each of these determinants are also presented with potential treatments, with the prerequisite of early detection.

**Mission Possible: Advances in MYC Therapeutic Targeting in Cancer**

The targeted concept of this journal is the MYC transcription factor, which is often referred to as a “master regulator”. Orthodoxically, the MYC family proteins regulate many important cellular processes, such as CAM junctions (adhesion), proliferation of cells, and general cell maintenance. Deregulation of MYC is observed in cancer patients, and it is now generally accepted that cancer increases deregulation of MYC through amplification. This deregulation caused by cancer increases the proliferation of the cancer itself, so it is common to see cancer increasing MYC activity. This journal explores potential treatments to MYC deregulation as well.

**Recent Progress**

There are many novel ideas that are still being tested between both journals. Combatting drug resistance with targeted therapies has an offered solution for many drug resistance determinants:

**Treatments to tumor burden and heterogeneity:**

A fundamental rule of thumb for tumor burden is the reciprocal relationship between tumor size and curability; the more cells a tumor has, the harder it is to treat. This also ties into mutation rate, if a tumor is growing rapidly, then it is also dividing and mutating rapidly, which means a higher chance of developing defenses against therapies. Currently, dose-dose therapy is a potential counter to this. Dose-dose therapy is a change in dosage scheduling; by giving a patient the effective amount of dosage in the shortest time possible, the tumor has a smaller chance of regrowth between dosages. Admittedly, this doesn’t make ineffective treatments effective, but there have been cases of stronger resolutions when compared to a patient without dose-dose therapy (Allen-Petersen et al. 2019).

**Treatments to physical barriers:**

Sanctuary sites are physical areas in the body that do not respond to treatment properly. Often times these sanctuary sites are synthesized by cancer itself by creating gradients within a tumor. The central nervous system (CNS) has a massive problem with sanctuary sites because the blood brain barrier often imposes treatment. Unfortunately, there is no specific treatment to sanctuary sites in the CNS currently. However, there are developments of understanding how exactly the blood brain barrier is impeding the treatment, which can ultimately result in a targeted therapy (Allen-Petersen et al. 2019).

**Treatments to tumor microenvironment:**

Tumor microenvironments is the environment surrounding a tumor, and often time allow cancerous cells to evade immunological responses. Currently, techniques that help detect the microenvironments are being developed. These techniques mix checkpoint blockades and other anti-angiogenic agents (Allen-Petersen et al. 2019).

**Undruggable genomic drivers:**

MYC deregulation and dimerization are both contributors to tumorigenesis. While there are many other genomic drivers that contribute to cancerous activity, such as P53 and RAS, the one that is dominantly focused on in both journals is MYC, because MYC is prolific in the body. MYC is undruggable because they lack regions that would respond to therapeutic inhibition. Recently, mini proteins have been offered as a possible solution to this, although this is widely untested. MYC transcription inhibition is a potential answer as well, which can be performed using OmoMYC, which is another expression for MYC that can be activated through switchable transgenes. Initially, inhibiting MYC would seem to have a plethora of negative implications, since it is responsible for so many cellular processes (Vasan et al. 2019). However, in mice, inhibiting transcription of MYC with OmoMYC expression resulted in little to no backlash, with dramatic loss in tumor composition. Additionally, OP449, a SET inhibitor, has shown to decrease MYC activity in breast cancer (Vasan et al. 2019). These studies are vital, because they show that MYC activity, while extremely complex, is amenable.

**Discussion**

The authors of these journals all propose a plethora of cunning and novel approaches to tumor reduction and drug resistance, but all of them should be taken with dubiousness. It is important to emphasize that every single one of these treatments must have a prerequisite of finding the tumor early, which is an entirely different and equally complex discussion as the discussions about treatment. The problem with early treatment is that these therapies can often result in exacerbating a problem that initially minimal because the tumor was benign. Additionally, many of these treatments aren’t exactly treatments, rather peripheral and secondary options that are to be complimented with orthodox therapies. For example, as helpful as the dose-dose therapy is, it simply increases efficacy rates of deterring tumor burden, but it doesn’t make an ineffective treatment effective.

While this may sound critical, there are certainly many advantages to both of these journals. It is true that the solutions they provide feel somewhat anti-climactic, it isn’t the treatments they often focus on, but the findings. The research in these studies are undoubtedly insightful and will ultimately help future researchers reach farther distances because of their work. For example, the MYC transcription factor was deemed “undruggable” by past researchers, yet the OmoMYC managed to reduce MYC activity and prevent deregulation.

Cancer is a multifaceted problem that will realistically require targeted solutions. These journals have helped dive deeper into finding those precise solutions by enumerating the problems and providing more intel to researchers.

**References**

Allen-Petersen, B. L., & Sears, R. C. (2019). Mission possible: advances in MYC therapeutic targeting in cancer. *BioDrugs*, *33*(5), 539-553.

Vasan, N., Baselga, J., & Hyman, D. M. (2019). A view on drug resistance in cancer. *Nature*, *575*(7782), 299-309.

Shlomai, G., Zelenko, Z., Antoniou, I. M., Stasinopoulos, M., Tobin-Hess, A., Vitek, M. P., ... & Gallagher, E. J. (2017). OP449 inhibits breast cancer growth without adverse metabolic effects. *Endocrine-related cancer*, *24*(10), 519-529.