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CANCER TREATMENT OPTIONS AND MANAGEMENT: PERSONALIZED NUTRACEUTICAL DIET PLAN

SYNTHETIC LETHALITY:

- Based on differences in the DNA damage response pathways between normal and cancer cells. See Fig 1.
- Cancer cells having less functional DNA repair compared to normal cells.
- Cancer cells rely on error-prone pathways, leading to higher mutation rates and genomic instability.
- Both radio and chemotherapy function by inducing DNA damage.
- Cancer cells can increase activity of DNA damage pathways in response to chemo/radiation therapy, making them resistant to treatment.
- Synthetic lethality is based on inhibiting these pathways during chemo/radiation treatment.
- Histone deacetylase (HDAC) over-expression in cancer cells can protect these cells from chemo/radiation.
- HDAC inhibitors can re-activate silenced tumor suppressor genes, interfere with DNA damage protection by activating the DNA damage checkpoint pathways (such as ATM) resulting in apoptosis (programmed cell death).
- Dietary agents (nutraceuticals) can trigger DNA damage response by modulating HDAC activities. See Fig 2.

A sustained DNA damage response coupled with insufficient DNA repair can selectively induce apoptosis in tumor cells while leaving normal cells intact (Rajendran et al., 2011).

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RATIONALE:

Triple Negative Breast Cancers (TNBC's) Are Characterized by Altered DNA Repair:

- TNBC's show a similar molecular profile to basal like tumors and BRCA1 deficient tumors. BRCA1 is activated in response to DNA damage (Lehmann et al., 2012).
- TNBC's are sensitive to inhibition of PARP1, a DNA repair protein that is activated in the presence of DNA damage (Hiller & Chu, 2012).
- TNBC's exhibit an abundance of DNA aberrations, suggesting that their DNA repair mechanisms/checkpoints are defective (Fornier & Fumoleau, 2011).
- TNBC's have defective DNA repair checkpoints (p53, ATM) (Shah et al., 2012).

TNBC's Respond to HDAC Inhibitors:

- Largazole is a HDAC1 inhibitor. Studies indicate that a combination of dexamethasone and Largazole cooperated to suppress cellular invasion of TNBC's in-vitro (Law et al., 2012).
- A recent study shows that co-treatment of TNBC cells and implanted xenografts with a combination of chloroquine and the pan-HDAC inhibitor panobinostat, resulted in superior inhibitory effects on cell growth and TNBC xenografts (Rao et al., (2012).

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Figure 1.

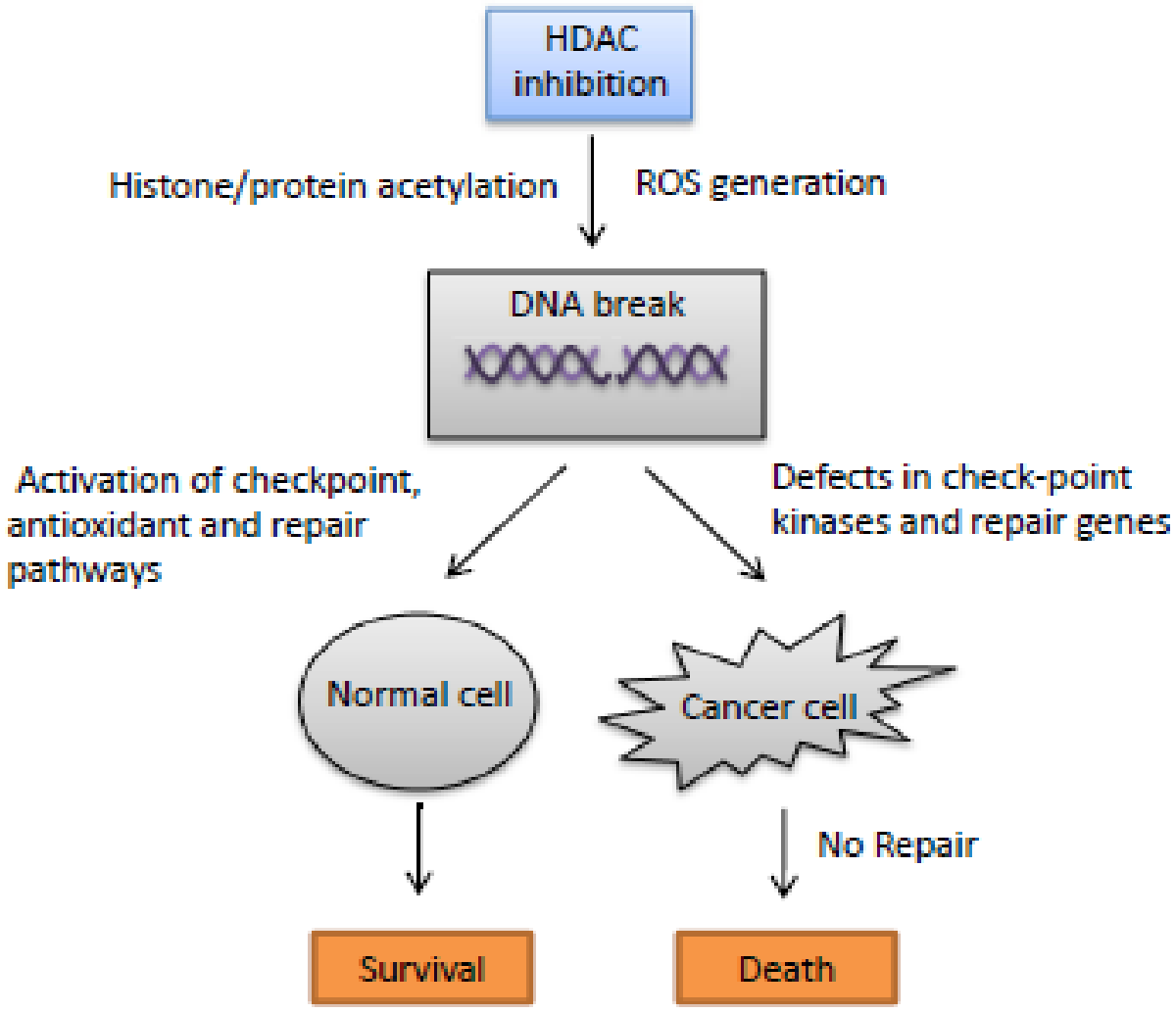

FIGURE 1: The differential effect of DNA damaging agents in cancer and normal cells.
HDAC inhibitors are known to cause DNA double strand breaks (DSBs) through chromatin remodeling and oxidative damage due to reactive oxygen species (ROS) generation. Normal cells counteract this by checkpoint activation leading to cell cycle arrest, anti-oxidant mechanisms and effective DNA repair, whereas cancer cells known to be defective in some of these mechanisms (check point kinases and repair genes), fail to repair the DNA damage leading to cell death (Rajendran et al., 2011).

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Figure 2.

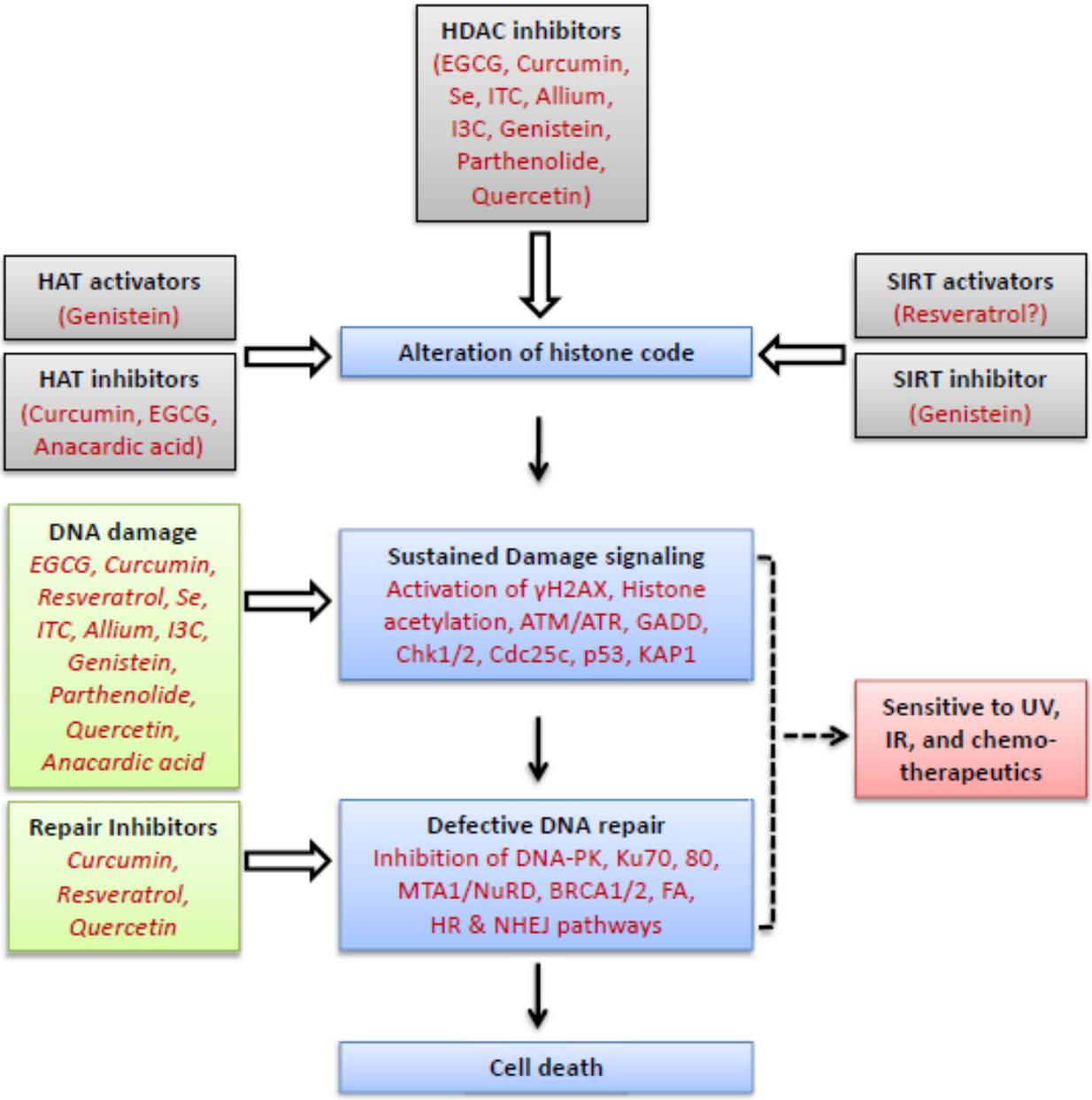

FIGURE 2: Dietary agents that sensitive tumor cells with defective DNA repair to geno-toxic (radiation/chemotherapy) regimes (Rajendran et al., 2011).

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DIETARY SUGGESTIONS:

NOTE: Please consult with physician BEFORE taking these or any other supplements as they may be contraindicated with your current prescription drugs.

Supplements:

- Curcumin 1000 - 1500mg/day
- Quercetin 1000 – 1500mg/day
- Bioperine 20 – 40mg/day
- Resveratrol 1000 – 1500 mg/day
- Green Tea extracts (EGCG) 1000 - 1500mg (of EGCG)/day
- Vitamin C - 1000mg/day

Take all supplements at the same time for 4-5 days in a row and then skip a day.

Also include as many of the following nutraceuticals daily if possible:

Isothiocyanate (ITC)

- Found in broccoli, watercress, wasabi, horseradish, mustard, radish, brussel sprouts, nasturtiums and capers.

Indole-3-carbinol (I3C)

- Found in cruciferous vegetables, broccoli, cabbage, cauliflower, brussel sprouts, collard greens and kale. I3C is also available as a dietary supplement – Take as directed.

Parthenolide (Feverfew)

- Supplement Form – Take as directed.

Allium

- Found in garlic, onions, shallots, leeks and chives.

Anacardic acid

- Found in cashew nutshell liquid (Supplement form – take as directed), cashews and mangoes.

Selenium (Se)

- Found in brazil nuts (best source), tuna, crab and lobster.
- Also available as a dietary supplement – take as directed.

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REFERENCES:

Fornier & Fumoleau, (2012). The paradox of triple negative breast cancer: novel approaches to treatment. Breast J; 18(1): 41-51.

Hiller & Chu, (2012). Current Status of Poly(ADP-ribose) Polymerase Inhibitors as Novel Therapeutic Agents for Triple-Negative Breast Cancer. Int J Breast Cancer; 2012: 829315: 6.

Law et al., (2012). Glucocorticoids and histone deacetylase inhibitors cooperate to block the invasiveness of basal-like breast cancer cells through novel mechanisms. Oncogene; doi: 10.1038/onc.2012.138. [Epub ahead of print]

Lehmann et al., (2012). Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. J Clin Invest; 121(7): 2750-67.

Rajendran et al., (2011). Dietary phytochemicals, HDAC inhibition, and DNA damage/repair defects in cancer cells. Clin Epigenetic; 3(1): 4.

Rao et al., (2012). Combination of pan-histone deacetylase inhibitor and autophagy inhibitor exerts superior efficacy against triple-negative human breast cancer cells. Mol Cancer Ther;11(4):973-83.

Shah et al., (2012). The clonal and mutational evolution spectrum of primary triple-negative breast cancers. Nature; doi: 10.1038/nature10933. [Epub ahead of print]