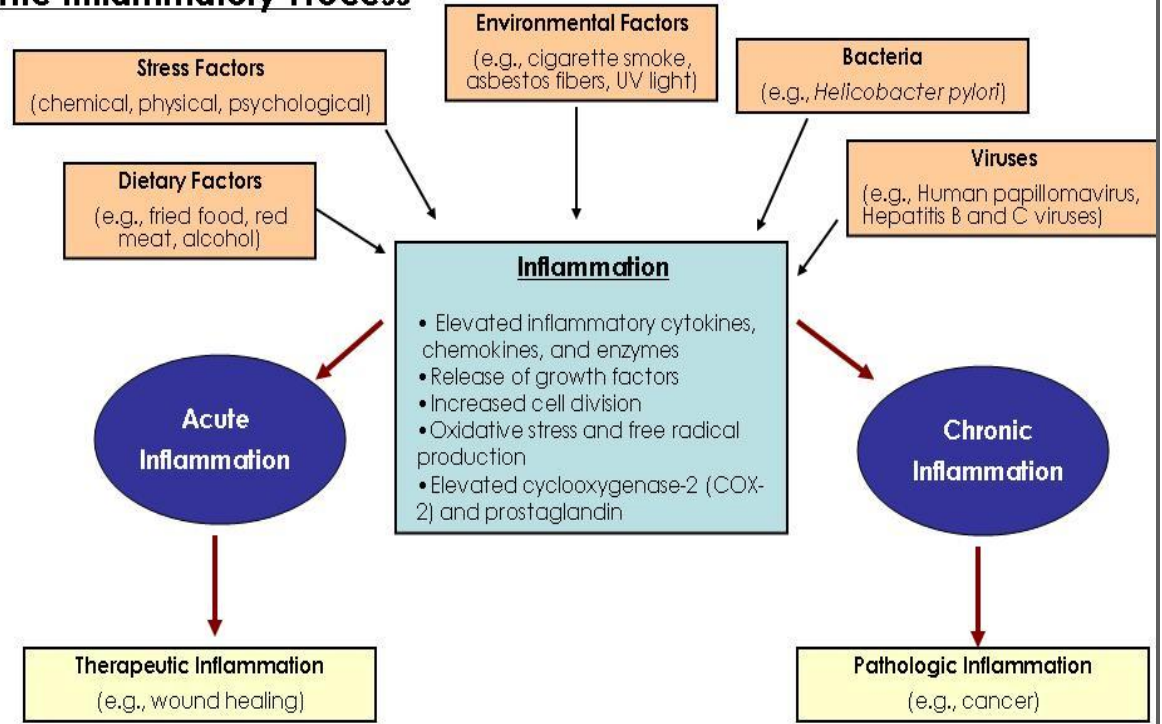


Inflammation-Cancer Link

The Inflammatory Process



Adapted from Aggarwal, B. et al. *Biochemical Pharmacology*, 2006.

Many chronic inflammatory conditions are associated risk factors for cancer (e.g., obesity, diabetes, and inflammatory bowel disease). Chronic inflammation may both predispose tissue to cancer and contribute to cancer progression and metastasis.

In addition to inflammation being associated with increased risk for developing cancer and cancer progression, research has shown that elevated markers of inflammation are associated with poor prognosis among those with cancer.

The inverse association between long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs) and the reduced risk of several cancers further supports the inflammation-cancer link.

Generally, we understand inflammation to be an acute defense response to tissue irritation, injury or infection. Acute inflammation, characterized by pain, redness, and swelling, is intended to be

protective and aid in wound healing. When inflammation is chronic, however, the inflammatory process may become pathogenic. Inflammation may become chronic either because an inflammatory stimulus persists (obesity) or because the inflammatory process becomes dysregulated and does not "turn off". The figure above depicts the pathways mediating acute and chronic inflammation. A variety of factors can cause inflammation. Subsequently, the inflammatory process may be acute or chronic depending on the stimuli causing inflammation and host conditions.

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Inflammation-Cancer Link continued....

Inflammation and Cancer Initiation

Stimuli, factors or conditions (e.g. obesity) that can lead to chronic inflammation increase risk for cancer by increasing the likelihood of DNA mutations. The inflammatory process causes oxidative stress and free radical production that can lead to DNA damage in the surrounding cells. Additionally, the inflammatory process increases cell division, increasing susceptibility to cell mutations.

Inflammation and Cancer Progression

It is generally accepted that chronic inflammation promotes tumor growth. The exact way in which inflammation encourages tumor growth, however, remains uncertain, but is likely multifactorial.

Chronic inflammation may contribute to tumor progression and growth by creating a pro-inflammatory environment conducive to the development of cancer. The inflammatory cytokines and enzymes triggered by the inflammation process facilitate cancer progression, thereby supporting tumor cell survival, tumor cell proliferation, and tumor cell invasion.

Furthermore, proinflammatory cytokines potentiate angiogenesis and enable metastases. That is, by inflammatory factors contributing to angiogenesis tumor cells are nourished via blood supplies. Consequently, these tumor cells are able to invade nearby tissues and spread to other parts of the body.

Inflammation and Breast Cancer

Several lines of evidence suggest a role of inflammation in the cause of breast cancer development. For example, elevated markers of inflammation have been associated with reduced overall survival in breast cancer patients. Furthermore, animal studies have consistently shown that NSAIDs (non-steroidal anti-inflammatory

Glossary

Acute inflammation– The initial response of the body to harmful stimuli characterized by redness, swelling, pain and/or heat. This is a protective reaction to injury, disease, or irritation of the tissues.

Angiogenesis– Blood vessel formation. Tumor angiogenesis is the growth of new blood vessels that tumors need to grow.

Cancer Initiation– The process by which normal cells are transformed into cancer cells.

Cancer Progression– Spreading or growing of the cancer cells.

Chronic inflammation– Prolonged inflammation that leads to a progressive shift in the type of cells that are present at the site of inflammation and is characterized by simultaneous destruction and healing of the tissue from the inflammatory process.

Metastases– The spread of cancer from one part of the body to another.

NSAID– A non-steroidal anti-inflammatory drug such as aspirin or ibuprofen.

Oxidative Stress– A condition of increased oxidant production in animal cells characterized by the release of free radicals and resulting in cellular degeneration.

Pathogenic– Capable of causing disease.

drugs) inhibit cancer development in breast cells and epidemiologic data provide evidence that NSAIDs may be associated with a reduced risk of breast cancer. Two recent meta-analyses found that overall, NSAID and aspirin use were associated with a 13% reduction in breast cancer risk.



Statins and Breast Cancer

Statins are a group of cholesterol lowering drugs that are widely used throughout the population to prevent several cardiovascular outcomes (e.g. stroke). Research suggests statins may also have a role in breast cancer prevention.

Although studies evaluating breast cancer and statin use have mixed findings, the largest published study designed specifically to look at statin use on estrogen receptor-negative (ER-) breast cancer found a 37% reduction in ER- breast cancers among women taking lipophilic statins for more than one year.

A recent study including women diagnosed with DCIS or stage 1 breast cancer found that fluvastatin decreased tumor proliferation and increased cell death in these tumors. These findings support a role for statins in breast cancer prevention.

The mechanism of cancer prevention associated with statin use is unclear. Several hypotheses exist. The effects of statins

on inflammation and immune modulation are potential pathways in which statins could prevent cancer.

The HRBP's "*Statins and Breast Cancer Biomarkers*" study was developed to further explore the potential relationship between statin

use and breast cancer prevention. This study randomizes premenopausal women to 1 year of atorvastatin (also known as Lipitor) or placebo and measures the effects on several markers of breast cancer risk including mammographic breast density.

Additional information on this study can be found on the HRBP website or by contacting Fonda Kingsley at 802-656-8502.



Updates on Funding Support for the HRBP

We would like to extend our appreciation and gratitude to all of the women in the HRBP and to those who help support the program through donations. Through grass roots efforts the HRBP has become more visible in the community as an important contributor to breast cancer research. In return, supporters have made donations to help fund the program.

Most recently, **Christina Reiss** from Essex Junction, Vt donated \$1000 to the HRBP.

Michael Cain of Fairfax, Vt participated in the 2009 Adirondack Canoe Classic, '90-Miler'. Mike and his family have been personally touched by breast cancer. Based on their positive experiences with FAHC during treatment, Mike wanted to contribute to breast cancer research here in Vermont. Mike raised \$654 for the HRBP!

Angela Smith of Burlington, Vt and pilates instructor for **Classic Form Pilates** hosted *Stretch for a Cure* benefit classes during the month of October. Proceeds were donated to the HRBP.

Once again the **HRBP Scarf Project** is selling scarves at the FAHC Breast Care Center and at UVM's Growing Vermont in the Davis Center. All proceeds support the HRBP and now is a great time to purchase scarves- they make for great holiday gifts!

If you are interested in donating to the HRBP you can do so through our website or by contacting Fonda Kingsley.



Mike Cain paddles in the Adirondack 90-Miler and raises money for breast cancer research in Vt.

H R**B P**

HIGH RISK
BREAST
PROGRAM
OF VERMONT

Fall 2009

High Risk Breast Program
Given E214
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Curried Butternut, Chicken and Apple Soup

Ingredients

3-4 pounds butternut or other winter squash
2 split chicken breasts
2 quarts chicken broth
2 tablespoons oil
2 cups chopped onion and or leeks
3 cloves garlic, peeled and chopped
3 cups apples, peeled, cored and diced
(about 4 apples)
3 tablespoons curry powder
1 slice bread, crusts removed
One-half cup cream (optional)
Chopped parsley
Salt and pepper

- ◆ Steam squash for 10 minutes or until the skin is soft. Let cool and then peel, seed and dice the flesh.
- ◆ Bring chicken stock to a boil in a medium sized pot. Submerge the chicken breasts and poach for 10 minutes or until cooked through. Remove the chicken and let cool. Discard the skin and bones. Dice the meat and set aside.
- ◆ In a large pot, heat the oil and add the onions, leeks and garlic. Sauté on medium heat for several minutes, then add the squash and apples. Continue to cook until the onions are translucent. Add the curry powder and a few teaspoons of salt and cook another minute. Add the broth and bread and raise the heat until it comes to a boil. Reduce to a simmer and cook about 20 minutes or until vegetables are soft.
- ◆ Remove from heat and puree in batches in a blender.

