

*Tamoxifen for breast cancer treatment is prescribed for years. The length of treatment coupled with side effects, such as menopausal symptoms, can make it tough to complete tamoxifen therapy. Dealing with menopausal symptoms related to hormone therapy can be hard.*

Find articles by Ka-Man V. Poueymirou Find articles by William T. Kline Find articles by William O. Stitt Find articles by Trevor N. Economides Find articles by Aris N. Yancopoulos Find articles by George D. Glass Find articles by David J. Glass Regeneron Pharmaceuticals, Inc. Received Jun 14; Accepted Aug 2. Abstract Skeletal muscle atrophy is a severe morbidity caused by a variety of conditions, including cachexia, cancer, AIDS, prolonged bedrest, and diabetes. One strategy in the treatment of atrophy is to induce the pathways normally leading to skeletal muscle hypertrophy. The pathways that are sufficient to induce hypertrophy in skeletal muscle have been the subject of some controversy. Upon induction of Akt in skeletal muscle, there was also a significant decrease in adipose tissue. These findings suggest that pharmacologic approaches directed toward activating Akt will be useful in inducing skeletal muscle hypertrophy and that an increase in lean muscle mass is sufficient to decrease fat storage. Skeletal muscle mass is increased in response to positive changes in workload or activity as a result of hypertrophy of individual muscle fibers, but the key molecular mediators of hypertrophy are only beginning to be elucidated Induction of hypertrophy in adult skeletal muscle is accompanied by the increased expression of insulin-like growth factor 1 IGF-1 7 , When IGF-1 levels were enhanced by using a muscle-specific promoter in transgenic mice, increased muscle size resulted 4 , Also, the addition of IGF-1 in vitro to differentiated muscle cells promotes myotube hypertrophy 9 , 18 , 19 , supporting the idea that hypertrophy can be mediated by pathways activated by autocrine or paracrine sources of IGF The binding of IGF-1 to its receptor triggers the activation of several intracellular kinases, including phosphatidylinositolkinase PI3K. Cell growth and survival in a variety of tissues and cell types in response to IGF-1, insulin, and other growth factors is mediated by Akt 6 , Indeed, induction of protein synthesis seems to be a key mechanism for inducing muscle fiber hypertrophy During adaptive hypertrophy in adult muscle and in IGF-induced myotube hypertrophy, Akt is phosphorylated and activated 2. Expression of constructs, via electroporation, encoding constitutively active forms of either PI3K or Akt induced muscle fiber hypertrophy both in vivo 2 , 16 and in vitro 18 , Mice in which Akt has been genetically disrupted display growth defects 3 , and those in which Akt and a related gene, Akt2, are both disrupted undergo skeletal muscle atrophy However, to date, transgenic animals have not been produced expressing constitutively active Akt c. Akt in skeletal muscle, nor has Akt been conditionally activated in the adult animal, as a way to test whether its activation is sufficient to induce hypertrophy. We describe here the production of such transgenic animals and demonstrate a novel method for inducing conditional transgenic tissue-specific expression in an adult animal. Southern blotting and by PCR. The amount of DNA recombination detected on the Southern blot was quantified by densitometry.

**Chapter 2 : Tamoxifen – the Cancer Drug that CAUSES Cancer**

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A recent trial showed that side effects, including vomiting and nausea, where have been linked with tamoxifen, may also occur in patients who take a placebo. Incidentally, tamoxifen is a generic name and not a brand name. And so the medical profession has concluded that tamoxifen may not be directly responsible for the vomiting and the nausea. So, the plan is to help doctors persuade more women to stick with the drug. This is utter madness – complete lunacy. Because, although tamoxifen is prescribed to treat breast cancer, it can cause uterine cancer. So women who take tamoxifen because they have breast cancer may also develop cancer of the womb. And perfectly healthy women who take tamoxifen because they worry that they might develop breast cancer could develop uterine cancer as a result of the tamoxifen. The medical world has gone mad. Tamoxifen is prescribed for patients who have had breast cancer and for those who are thought to be specially likely to develop it. Last year a terrifying , prescriptions were dispensed for tamoxifen. But nearly a third of patients who take the drug give up taking it because of the unpleasant side effects. In addition to vomiting and nausea, the drug also causes hot flushes, sweating and low libido. Now doctors want patients to ignore the side effects – and take the drug anyway. Twenty years ago I was the first doctor to reveal the truth about tamoxifen. There were plans to give tamoxifen to every woman in the country. But my revelations stopped those plans. Now doctors are trying to give tamoxifen a boost again. There are hundreds of free articles on www. But not a lot.

**Chapter 3 : Tamoxifen | Radiology Key**

*8 Tamoxifen. Beverly G. Coleman. Although this chapter is somewhat unique in the sense that the title does not describe a particular clinical symptom, the subject matter is extremely relevant and important because tamoxifen remains the most widely prescribed endocrine therapy for breast cancer.*

**Abstract** The published literature comparing surgery, with or without adjuvant endocrine therapy, with endocrine therapy alone in older women with operable breast cancer was systematically reviewed. The design used is Cochrane review. Eligible studies recruited women aged 70 years or over with operable breast cancer, fit for surgery under general anaesthesia. The studies compared surgery either mastectomy or wide local excision, with or without endocrine therapy to endocrine therapy alone. Double data extraction and quality assessment were undertaken. Seven eligible trials were identified of which six had published time-to-event data. The quality of the allocation concealment was adequate in three studies and unclear in the remainder. In each case the endocrine therapy used was tamoxifen. When surgery alone was compared to endocrine therapy alone, there was no significant difference in OS hazard ratio HR 0. When surgery with adjuvant endocrine therapy was compared to endocrine therapy alone, there was no significant difference in OS HR 0. The regimens have different side effect profiles with one study suggesting increased psychosocial morbidity at 3 months in the surgical arm, which resolves by 2 years. Primary endocrine therapy with tamoxifen is associated with inferior local disease control but non-inferior survival to surgery for breast cancer in older women. Trials are needed to evaluate appropriate selection criteria for its use in terms of patient co-morbidity and quality of life. Trials are needed to evaluate the clinical effectiveness of aromatase inhibitors as primary therapy for this population. Primary endocrine therapy was first described in the early s as an alternative for older women Preece et al, Treatment involved the sole use of tamoxifen, an oestrogen-receptor antagonist, without surgery, radiotherapy or chemotherapy. In the UK, the trend towards treating women aged 70 and over with tamoxifen alone has been based on the premise that they are less likely to be fit for surgery because of co-morbidity Satariano and Ragland, However, both mastectomy and wide local excision have low mortality rates Hunt et al, ; Wyld and Reed, Breast surgery-related morbidity, especially where axillary surgery is involved, is quite high and may impact on quality of life. Primary endocrine therapy is not a treatment option in the USA and is rarely used in Australia Craft et al, ; Diab et al, To establish whether primary endocrine therapy is justifiable for women who are fit for surgery, we systematically reviewed the evidence from randomised trials comparing primary endocrine therapy to surgery, with or without adjuvant endocrine therapy, in the management of women aged 70 years or over with operable breast cancer. Only controlled trials with the following characteristics were included. Participants were women aged 70 years or over with clinically defined operable primary breast cancer: Studies had to compare either 1 surgery alone vs primary endocrine therapy; or 2 surgery plus adjuvant endocrine therapy vs primary endocrine therapy. Mastectomy could be with or without axillary clearance, and wide local excision could be with or without radiotherapy. Primary outcomes were overall survival OS and progression-free survival PFS interval between start of treatment and need for second-line or palliative treatment, recurrence or death from any cause. Secondary outcomes were adverse effects number of surgical complications or endocrine therapy related side effects , local disease control interval between start of treatment and the development of local disease , distant metastasis-free interval interval between start of treatment and the development of metastatic disease and quality of life however measured. Pre-specified subgroups included the type of surgery mastectomy or wide local excision, with or without radiotherapy. Two reviewers, LW and DH, independently assessed each potentially eligible trial for inclusion in the review with the results section masked. The same two reviewers independently reviewed each study according to its design and by how the study was conducted to assess any bias. The checklist for quality of randomised controlled trials included: The most complete data set feasible was assembled from the published literature. Where necessary, we sought additional information from the principal investigator of the trial concerned. Results of eligible studies were statistically synthesised if appropriate and possible. Absolute risk reductions and numbers needed to treat were calculated using the Altman and Andersen method. Of these,

were excluded based on information in the title or abstract. The remaining 28 citations reported on the seven potentially eligible studies for the review. None of these studies was excluded. Five additional papers, all conference abstracts, relating to the same trials were identified through informal reference tracking and contact with authors.

#### Chapter 4 : Coleman, Beverly G.

*Coleman, Beverly G. Emeritus Professor CE Current Positions. Emeritus Professor CE of Radiology, Department of Radiology, Perelman School of Medicine - Publications.*

#### Chapter 5 : Reviews of Beverley Coleman, Real Estate Agent in Martinsville | Trulia

*Mustacchi G, Ceccherini R, Milani S, Pluchinotta A, De Matteis A, Maiorino L, Farris A, Scanni A, Sasso F, Italian Cooperative Group GRETA Tamoxifen alone vs adjuvant tamoxifen for operable breast cancer of the elderly: long-term results of the phase III randomized controlled multicenter GRETA trial.*

#### Chapter 6 : Conditional Activation of Akt in Adult Skeletal Muscle Induces Rapid Hypertrophy

*The pharmaceutical company AstraZeneca is the maker of the drug tamoxifen. According to "Pink Ribbon Culture," AstraZeneca gave \$97, to Komen affiliates in They have been known to have a very large presence at Komen "race for the cure" events and they have been a major force in Breast Cancer Awareness Month.*