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Topics of interest:

Small molecule drugs that target the sirtuins, a recently discovered family of seven enzymes associated with the aging process

Dr. Christoph Westphal has emerged as a dynamic leader of calorie restriction research – increasing the likelihood that we will soon learn whether the ancient defense system that empowers living organisms to weather times of food scarcity can be harnessed to benefit human health and longevity. For years, scientists have talked about creating a CR mimetic. Now, Dr. Westphal has made that much more predictable. Seeking the world's greatest scientists for collaboration, he formed a partnership with Dr. David Sinclair. Together they created Sirtris, a cutting-edge biotech company that creates disease-intervention pharmaceuticals that change the activity level of sirtuin genes.

Most biotech startups burn through their cash, never realizing their ideas – even if worthy. With Dr. Wesphal's leadership, Sirtris rocketed from biotech startup to a welcome acquisition by GSK. This corporate connection is vitally important because now Dr. Westphal and the great team he has assembled have the financial backing to explore fully the potential of the Sirtuin genes for drug discovery. By further elucidating how CR science works, they will benefit millions.

The leader of this important mission must be the rare individual who has a deep background in medical research and genetics so that effective research paths will be chosen, as well as the business acumen to generate the support to move forward. Dr. Christoph Westphal is this gifted leader.

PUBLICATIONS

Crystal structures of human SIRT3 displaying substrate-induced conformational changes.

Jin L, Wei W, Jiang Y, Peng H, Cai J, Mao C, Dai H, Choy W, Bemis JE, Jirousek MR, Milne JC, Westphal CH, Perni RB.

Journal of Biological Chemistry. 2009 Sep 4;284(36):24394-405. Epub 2009 Jun 16.PMID: 19535340

Biochemical characterization, localization, and tissue distribution of the longer form of mouse SIRT3. Jin L, Galonek H, Israelian K, Choy W, Morrison M, Xia Y, Wang X, Xu Y, Yang Y, Smith JJ, Hoffmann E, Carney DP, Perni RB, Jirousek MR, Bemis JE, Milne JC, Sinclair DA, Westphal CH.

Protein Science. 2009 Mar;18(3):514-25.PMID: 19241369

Small molecule activators of SIRT1 as therapeutics for the treatment of type 2 diabetes.

Milne JC, Lambert PD, Schenk S, Carney DP, Smith JJ, Gagne DJ, Jin L, Boss O, Perni RB, Vu CB, Bemis JE, Xie R, Disch JS, Ng PY, Nunes JJ, Lynch AV, Yang H, Galonek H, Israelian K, Choy W, Iffland A, Lavu S, Medvedik O, Sinclair DA, Olefsky JM, Jirousek MR, Elliott PJ, Westphal CH. Nature. 2007 Nov 29;450(7170):712-6.PMID: 18046409

A therapeutic role for sirtuins in diseases of aging?

Westphal CH, Dipp MA, Guarente L. **Trends in Biochemical Sciences**. 2007 Dec;32(12):555-60. Epub 2007 Nov 5. Review.PMID: 17980602

Keeping it real with investors.

Dipp M, Westphal C, Mirkin C, Baker J, Harper T, Harris C. Nature Biotechnology. 2006 Feb;24(2):133-5. PMID: 16526102

Ataxia telangiectasia mutated expression and activation in the testis

Hamer G, Kal HB, Westphal CH, Ashley T, de Rooij DG. **Biology of Reproduction**. 2004 Apr;70(4):1206-12. Epub 2003 Dec 17.PMID: 14681204

Atm inactivation results in aberrant telomere clustering during meiotic prophase.

Pandita TK, Westphal CH, Anger M, Sawant SG, Geard CR, Pandita RK, Scherthan H. **Molecular and Cellular Biology**. 1999 Jul;19(7):5096-105.PMID: 10373558

The neuroendocrine protein 7B2 is required for peptide hormone processing in vivo and provides a novel mechanism for pituitary Cushing's disease.

Westphal CH, Muller L, Zhou A, Zhu X, Bonner-Weir S, Schambelan M, Steiner DF, Lindberg I, Leder P.

Cell. 1999 Mar 5;96(5):689-700.PMID: 10089884

Loss of atm radiosensitizes multiple p53 null tissues.

Westphal CH, Hoyes KP, Canman CE, Huang X, Kastan MB, Hendry JH, Leder P. **Cancer Research**. 1998 Dec 15;58(24):5637-9.PMID: 9865712

Atm-dependent interactions of a mammalian chk1 homolog with meiotic chromosomes.

Flaggs G, Plug AW, Dunks KM, Mundt KE, Ford JC, Quiggle MR, Taylor EM, Westphal CH, Ashley T, Hoekstra MF, Carr AM. **Current Biology**. 1997 Dec 1;7(12):977-86.

Cell-cycle signaling: Atm displays its many talents.

Westphal CH. Current Biology. 1997 Dec 1;7(12):R789-92. Review.

atm and p53 cooperate in apoptosis and suppression of tumorigenesis, but not in resistance to acute radiation toxicity.

Westphal CH, Rowan S, Schmaltz C, Elson A, Fisher DE, Leder P. **Nature Genetics**. 1997 Aug;16(4):397-401.PMID: 9241281

Transposon-generated 'knock-out' and 'knock-in' gene-targeting constructs for use in mice.

Westphal CH, Leder P. Current Biology. 1997 Jul 1;7(7):530-3.PMID: 9210379

Genetic interactions between atm and p53 influence cellular proliferation and irradiationinduced cell cycle checkpoints.

Westphal CH, Schmaltz C, Rowan S, Elson A, Fisher DE, Leder P. **Cancer Research**. 1997 May 1;57(9):1664-7.PMID: 9135004