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PH 240F
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Assignment 1

Question 2. Albinism.

		Father	
		A	a
Mother	A	AA	Aa
	a	Aa	aa

Let A = Dominant allele.
Whoever has this allele will not express the albino phenotype.

Let a = Recessive allele.
Whoever is homozygous for this allele will express the albino phenotype.

$$P(\text{both twins have same phenotype})$$

$$= P(\text{both not albino} \cup \text{both albino})$$

$$= P(\text{both not albino}) + P(\text{both albino})$$

$$= P(\text{twin 1 not albino})P(\text{twin 2 not albino})$$

$$+ P(\text{twin 1 albino})P(\text{twin 2 albino})$$

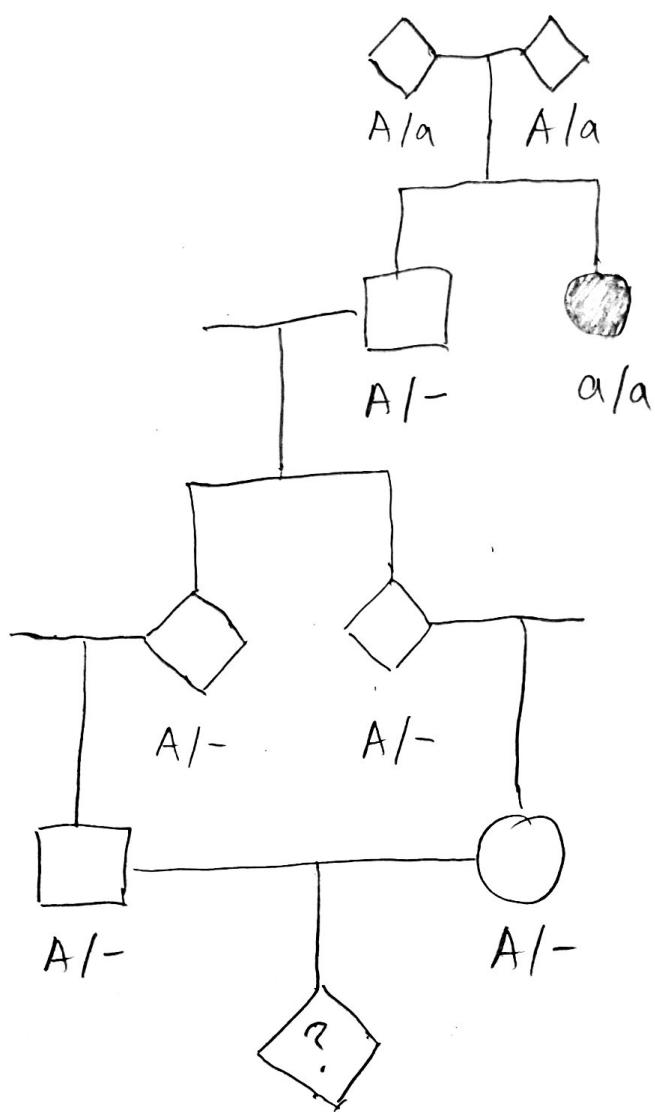
$$= [1 - P(aa)] [1 - P(aa)] + P(aa) P(aa)$$

$$= [1 - P(aa)]^2 + [P(aa)]^2$$

$$= \left(\frac{3}{4}\right)^2 + \left(\frac{1}{4}\right)^2 = \frac{9}{16} + \frac{1}{16} = \frac{10}{16} = \boxed{\frac{5}{8} = 0.625}$$

Question 3. Tay-Sachs Disease

a.



"A" represents the normal allele.

"a" represents the recessive allele that cause Tay-Sachs

Question 3. Tay-Sachs Disease (continued)

b. We need to find

$$P(\text{cousins' child has Tay-Sachs disease})$$

$$= P(\text{woman is A/a})P(\text{man is A/a})P(\text{cousins' child is a/a})$$

$$P(\text{woman is A/a}) = P(\text{Grandpa is A/a})$$

$$* P(\text{Grandpa's child/woman's parent is A/a})$$

$$* P(\text{woman is A/a})$$

$$P(\text{woman is A/a}) = \frac{2}{3} * \frac{1}{2} * \frac{1}{2}$$

$$P(\text{Grandpa is A/a}) = \frac{2}{3} \quad \text{because we know that}\\ \text{grandpa does not have}\\ \text{Tay-Sach's disease.}$$

$$P(\text{Grandpa's child/woman's parent is A/a}) = \frac{1}{2}$$

can be seen by the punnet square:

		Grandpa	
		A	a
Grandma	A	AA	Aa
	A	AA	Aa

Question 3 . Tay-Sachs Disease(continued)

b. $P(\text{woman is } A/a) = \frac{1}{2}$ can be seen by the punnet square:

Woman's parent from
grandpa's side

	A	a	
Woman's parent not from grandpa	A	AA	Aa
	A	AA	Aa

Similarly,

$$P(\text{man is } A/a) = P(\text{Grandpa is } A/a)$$

* $P(\text{Grandpa's child/man's parent is } A/a)$

* $P(\text{man is } A/a)$

$$= \frac{2}{3} * \frac{1}{2} * \frac{1}{2}$$

$P(\text{cousins' child is } a/a) = \frac{1}{4}$ can be seen with a
punnet square.

	A	a	
woman	A	AA	Aa
	a	Aa	aa

Question 3. Tay-Sachs Disease (continued)

b. Therefore,

$P(\text{cousins' child has Tay-Sachs disease})$

$$= P(\text{Woman is A/a}) P(\text{man is A/a}) P(\text{cousins' child is a/a})$$

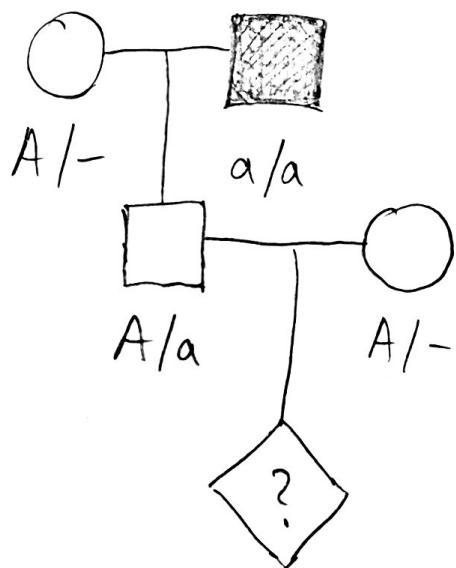
$$= \frac{2}{3} * \frac{1}{2} * \frac{1}{2} * \frac{2}{3} * \frac{1}{2} * \frac{1}{2} * \frac{1}{4}$$

$$= \frac{1}{144} = 0.00694$$

Question 4. Cystic Fibrosis

a. Let "A" be the normal dominant allele that does not cause cystic fibrosis.

Let "a" be the recessive allele that causes cystic fibrosis.



b. $P(\text{couple's first child has CF})$

$$= P(\text{man is } A/a) * P(\text{woman is } A/a) * P(\text{child is } a/a)$$

$$= 1 * \frac{1}{50} * \frac{1}{4} = \frac{1}{200} = 0.05$$

Question 4. Cystic Fibrosis (continued)

b. Explanation:

$P(\text{man is A/a}) = 1$ can be seen using a punnet square.

Man's Father

		a	a
Man's	A	Aa	Aa
Mother	a	aa	aa

Since it is given that the man is phenotypically unaffected, man must be A/a.

$P(\text{woman is A/a}) = \frac{1}{50}$ because the population frequency for cystic fibrosis is $1/50$.

$P(\text{child is a/a}) = \frac{1}{4}$ can be seen with a punnet square.

		Man	
		A	a
Woman	A	AA	Aa
	a	Aa	aa

Question 4. Cystic Fibrosis (continued)

c. If the first child has cystic fibrosis, it means the man's wife is A/a.

$$P(\text{2nd child is unaffected} \mid \text{1st child is } a/a) = \frac{3}{4} = 0.75$$

This can be seen using a punnet square:

		Man	
		A	a
Woman	A	AA	Aa
	a	Aa	aa

For the child to be unaffected, the child needs to be A/A or A/a. Hence the answer $\frac{3}{4} = 0.75$.

Question 5. Self-Pollination

Initially:

$$0.55 \text{ AA}$$

$$0.40 \text{ Aa}$$

$$0.05 \text{ aa}$$

1st Generation:

$$0.55 \text{ AA}$$

A	AA	Aa
a	Aa	aa

$$0.05 \text{ aa}$$

$$0.40\left(\frac{1}{4} \text{ AA}\right)$$

$$0.40\left(\frac{1}{2} \text{ Aa}\right)$$

$$0.40\left(\frac{1}{4} \text{ aa}\right)$$

$$\left[0.55 + 0.40\left(\frac{1}{4}\right)\right] \text{ AA}$$

$$0.40\left(\frac{1}{2}\right) \text{ Aa}$$

$$\left[0.40\left(\frac{1}{4}\right) + 0.05\right] \text{ aa}$$

$$= 0.65 \text{ AA}$$

$$= 0.20 \text{ Aa}$$

$$= 0.15 \text{ aa}$$

Question 5: Self-Pollination (continued)

2nd Generation:

$$0.65 \text{ AA}$$

A	A	a
A	AA	Aa
a	Aa	aa

$$0.15 \text{ aa}$$

$$0.20\left(\frac{1}{4} \text{ AA}\right)$$

$$0.20\left(\frac{1}{2} \text{ Aa}\right)$$

$$0.20\left(\frac{1}{4} \text{ aa}\right)$$

$$\left[0.65 + 0.2\left(\frac{1}{4}\right)\right] \text{ AA}$$

$$0.20\left(\frac{1}{2}\right) \text{ Aa}$$

$$\left(0.20\left(\frac{1}{4}\right) + 0.15\right) \text{ aa}$$

$$= 0.70 \text{ AA}$$

$$= 0.10 \text{ Aa}$$

$$= 0.20 \text{ aa}$$

3rd Generation:

$$\left[0.70 + 0.10\left(\frac{1}{4}\right)\right] \text{ AA}$$

$$0.10\left(\frac{1}{2}\right) \text{ Aa}$$

$$\left[0.10\left(\frac{1}{4}\right) + 0.20\right] \text{ aa}$$

$$= 0.725 \text{ AA}$$

$$= 0.05 \text{ Aa}$$

$$= 0.225 \text{ aa}$$

So after 3 generations, the proportions are

0.725 AA, 0.05 Aa, and 0.225 aa.

Question 6: Allele Frequency Estimation for a Mendelian Disease

Let X = number of affected individuals in a random sample of n individuals. This includes all individuals with DD and Dd genotypes.

DD has allele frequency p^2

Dd has allele frequency $2p(1-p)$

dd has allele frequency $(1-p)^2$

Let $n-X$ = number of unaffected individuals,

This is all the individuals with dd genotypes.

The likelihood function is the following:

$$f(X|p) = \binom{n}{X} [p^2 + 2p(1-p)]^X [(1-p)^2]^{n-X}$$

$$f(X|p) = \frac{n!}{X!(n-X)!} [p^2 + 2p(1-p)]^X [(1-p)^2]^{n-X}$$

Question 6: Allele Frequency Estimation for a Mendelian Disease (continued)

$$f(X|p) = \frac{n!}{X!(n-X)!} (2p-p^2)^X [(1-p)^2]^{n-X}$$

$$\ell(p) = \log(f(X|p)) = \log n! - \log X! - \log(n-X)! + X \log(2p-p^2) + 2(n-X) \log(1-p)$$

$$\ell(p) = \log n! - \log X! - \log(n-X)! + X \log(2p-p^2) + 2n \log(1-p) - 2X \log(1-p)$$

$$\frac{\partial \ell(p)}{\partial p} = \frac{X}{2p-p^2} (2-2p) - \frac{2n}{1-p} + \frac{2X}{1-p}$$

Note: There is no reason to use Lagrange multiplier because the constraint $p + (1-p) = 1$ is already part of $p^2 + 2p(1-p) + (1-p)^2 = 1$.

$$\frac{X}{2\hat{p}-\hat{p}^2} (2-2\hat{p}) - \frac{2n}{1-\hat{p}} + \frac{2X}{1-\hat{p}} = 0$$

$$\frac{2X}{2\hat{p}-\hat{p}^2} - \frac{2\hat{p}X}{2\hat{p}-\hat{p}^2} - \frac{2n}{1-\hat{p}} + \frac{2X}{1-\hat{p}} = 0$$

Question 6: Allele Frequency Estimation for a Mendelian Disease (continued)

$$\frac{2X - 2\hat{p}X}{2\hat{p} - \hat{p}^2} = \frac{2n - 2X}{1 - \hat{p}}$$

$$(2X - 2\hat{p}X)(1 - \hat{p}) = (2n - 2X)(2\hat{p} - \hat{p}^2)$$

$$2X - 2X\hat{p} - 2X\hat{p} + 2X\hat{p}^2 = 4n\hat{p} - 2n\hat{p}^2 - 4X\hat{p} + 2X\hat{p}^2$$

$$2X - \cancel{4X\hat{p}} + \cancel{2X\hat{p}^2} = 4n\hat{p} - 2n\hat{p}^2 - \cancel{4X\hat{p}} + \cancel{2X\hat{p}^2}$$

$$2X = 4n\hat{p} - 2n\hat{p}^2$$

$$X = 2n\hat{p} - n\hat{p}^2$$

$$n\hat{p}^2 - 2n\hat{p} + X = 0$$

$$n\hat{p}^2 - 2n\hat{p} = -X$$

$$\hat{p}^2 - 2\hat{p} = -\frac{X}{n}$$

$$\hat{p}^2 - 2\hat{p} + 1 = -\frac{X}{n} + 1$$

$$(\hat{p} - 1)^2 = 1 - \frac{X}{n}$$

$$\hat{p} - 1 = -\sqrt{1 - \frac{X}{n}} \quad \therefore \hat{p}_{MLE} = 1 - \sqrt{1 - \frac{X}{n}}$$

Part II. NCBI WWW Resources

Question 2. MapViewer

- Gene Symbol: DEC2 (also called BHLHE41, BHLHB3, bHLHe41, SHARP-1, SHARP1)
- Cytoband Location: 12p12.1
- Description: This gene encodes a basic helix-loop-helix protein expressed in various tissues. The encoded protein can interact with ARNTL or compete for E-box binding sites in the promoter of PER1 and repress CLOCK/ARNTL's transactivation of PER1. This gene is believed to be involved in the control of circadian rhythm and cell differentiation. Defects in this gene are associated with the short sleep phenotype.
- Relevant Map Portion on following page

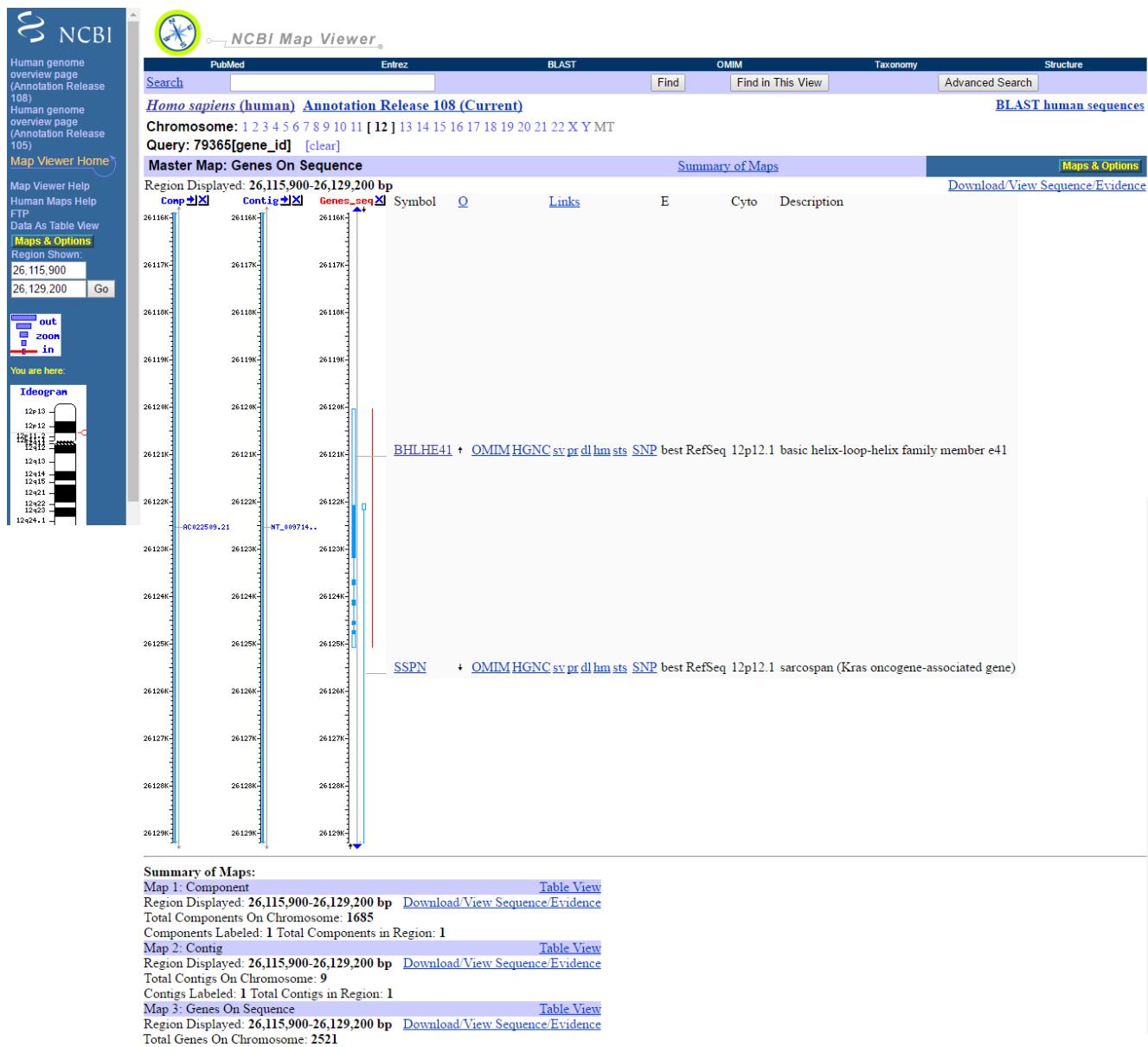


Figure 1: Relevant Map Portion from MapViewer

Question 3. GenBank

- GenBank Accession Number: NG_021173.1
- Length of Sequence: 12,045 basepairs linear DNA
- DNA Sequence on next page

Nucleotide

FASTA

Homo sapiens basic helix-loop-helix family member e41 (BHLHE41), RefSeqGene on chromosome 12

NCBI Reference Sequence: NG_021173.1

[GenBank](#) [Graphics](#)

>NG_021173.1 Homo sapiens basic helix-loop-helix family member e41 (BHLHE41), RefSeqGene

Question 4. PubMed

Dynamic circadian protein-protein interaction networks predict temporal organization of cellular functions.

- PMID: 23555304
- Abstract

[PLoS Genet.](#) 2013 Mar;9(3):e1003398. doi: 10.1371/journal.pgen.1003398. Epub 2013 Mar 28.

Dynamic circadian protein-protein interaction networks predict temporal organization of cellular functions.

Wallach T¹, Schellenberg K, Maier B, Kalathur RK, Porras P, Wanker EE, Futschik ME, Kramer A.

Author information

¹Laboratory of Chronobiology, Charité-Universitätsmedizin, Berlin, Germany.

Abstract

Essentially all biological processes depend on protein-protein interactions (PPIs). Timing of such interactions is crucial for regulatory function. Although circadian (~24-hour) clocks constitute fundamental cellular timing mechanisms regulating important physiological processes, PPI dynamics on this timescale are largely unknown. Here, we identified 109 novel PPIs among circadian clock proteins via a yeast-two-hybrid approach. Among them, the interaction of protein phosphatase 1 and CLOCK/BMAL1 was found to result in BMAL1 destabilization. We constructed a dynamic circadian PPI network predicting the PPI timing using circadian expression data. Systematic circadian phenotyping (RNAi and overexpression) suggests a crucial role for components involved in dynamic interactions. Systems analysis of a global dynamic network in liver revealed that interacting proteins are expressed at similar times likely to restrict regulatory interactions to specific phases. Moreover, we predict that circadian PPIs dynamically connect many important cellular processes (signal transduction, cell cycle, etc.) contributing to temporal organization of cellular physiology in an unprecedented manner.

PMID: 23555304 PMCID: [PMC3610820](#) DOI: [10.1371/journal.pgen.1003398](#)

[PubMed - indexed for MEDLINE] [Free PMC Article](#)

The rexinoid bexarotene represses cyclin D1 transcription by inducing the DEC2 transcriptional repressor.

- PMID: 20821348
- Contains the phrase "cell cycle" in abstract
- Abstract on following page

1. Breast Cancer Res Treat. 2011 Aug;128(3):667-77. doi: 10.1007/s10549-010-1083-9. Epub 2010 Sep 7.

The rexinoid bexarotene represses cyclin D1 transcription by inducing the DEC2 transcriptional repressor.

Li Y¹, Shen Q, Kim HT, Bissonnette RP, Lamph WW, Yan B, Brown PH.

Author information:

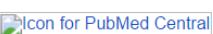
- ¹Department of Clinical Cancer Prevention, The University of Texas, Anderson Cancer Center Cancer, Houston, TX 77030, USA.

Abstract

Bexarotene is an RXR-selective vitamin A analog that has been shown to prevent ER-negative mammary tumorigenesis in animal models. While investigating the mechanism by which bexarotene prevents ER-negative breast cancer development, we found that the expression of cyclin D1, a critical cell cycle promoter, was repressed by bexarotene in vitro and in vivo. Time course and cycloheximide experiments show that repression of cyclin D1 is a late effect and requires new protein synthesis. Previously we discovered that DEC2 (differentially expressed in chondrocytes-2), a helix-loop-helix transcription repressor, was induced by bexarotene in human mammary epithelial cells. Therefore, we hypothesized that bexarotene represses the transcription of cyclin D1 through induction of DEC2. Luciferase reporter studies demonstrated that either bexarotene treatment or forced expression of DEC2 can repress the transcription of a cyclin D1 promoter reporter by affecting the basal transcriptional activity. Results from chromatin immunoprecipitation experiments showed that bexarotene treatment causes the recruitment of DEC2 and HDAC1 (histone deacetylase 1) to the cyclin D1 promoter. Co-immunoprecipitation confirms the interaction between DEC2 and HDAC1, suggesting that the recruitment of HDAC1 to the cyclin D1 promoter is through DEC2. Trichostatin A, a HDAC inhibitor, reverses the cyclin D1 repression by bexarotene, suggesting that repression of cyclin D1 involves histone deacetylation. Knock-down of DEC2 by siRNA abolishes the cyclin D1 repression, further supporting our hypothesis. Finally, we demonstrated that overexpression of DEC2 dramatically inhibited cell proliferation and repressed the expression of cyclin D1 in human mammary epithelial cells. These results suggest that bexarotene down-regulates cyclin D1 through induction of DEC2, followed by recruitment of HDAC1 to the cyclin D1 promoter causing transcriptional repression. By elucidating the mechanism by which rexinoids inhibit cell proliferation, it will be possible to develop more effective and less toxic drugs to prevent ER-negative breast cancers.

PMCID: PMC3444826 [Free PMC Article](#)

PMID: 20821348 [PubMed - indexed for MEDLINE]



Molecular cloning and characterization of DEC2, a new member of basic helix-loop-helix proteins.

- PMID: 11162494
- Contains the phrase "cell cycle" in abstract
- Abstract on following page

Item 1 of 1 ([Display the citation in PubMed](#))

1. Biochem Biophys Res Commun. 2001 Jan 12;280(1):164-71.

Molecular cloning and characterization of DEC2, a new member of basic helix-loop-helix proteins.

[Fujimoto K¹](#), [Shen M](#), [Noshiro M](#), [Matsubara K](#), [Shingu S](#), [Honda K](#), [Yoshida E](#), [Suardita K](#), [Matsuda Y](#), [Kato Y](#).

Author information:

- ¹Department of Biochemistry, Hiroshima University School of Dentistry, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8553, Japan.

Abstract

DEC1 is a basic helix-loop-helix (bHLH) protein related to Drosophila Hairy, Enhancer of split and HES, and involved in the control of proliferation and/or differentiation of chondrocytes, neurons, etc. We report here the identification and characterization of human, mouse and rat DEC2, a novel member of the DEC subfamily. DEC2 had high (97%) and moderate (52%) similarities in the bHLH region and the Orange domain with DEC1, respectively. However, DEC2, but not DEC1, had alanine and glycine-rich regions in the C-terminal half. Unlike Hairy, Enhancer of split and HES, DEC2 lacked the WRPW motif for interaction with the corepressor Groucho. The DEC2 gene was mapped to human chromosome 12p11.23-p12.1, mouse chromosome 6 G2-G3 and rat chromosome 4q43 distal-q4, where the conserved linkage homology has been identified among these species. Unlike DEC1, which was broadly expressed in many tissues, DEC2 showed a more restricted pattern of mRNA expression. The DEC subfamily proteins may play an important role in tissue development.

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PMID: 11162494 [PubMed - indexed for MEDLINE]

ELSEVIER
FULL-TEXT ARTICLE

No other abstracts had the phrase "cell cycle". No abstracts had the word "mitosis".