Personal DNA sequence modification: a potential new modality for gene transmission and therapy as well as mammalians evolution.

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Research note

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Abstract

Objective: Changes in DNA sequence are usually caused by viruses, certain chemicals and radiation as well as by transposons, somatic hyper mutation and errors during meiosis. We can consider gene therapy as an induced DNA sequence changes by inserting certain gene or genes, through viral vectors mainly. Anyhow, many problems met gene therapy like short-lived nature, need for multiple rounds of that therapy, immune response for gene or vector as foreigners, problems with viral vectors and malignancy induction. Wet nurse or foster suckling mother means breastfeeding an infant that is not one's biological offspring which was a job from ancient Egyptians times till the present. Results: Here we show a significant change in DNA sequence in babies after foster mothers suckling compared to their DNA before suckling foster mother suggesting presence of potential factors in foster mother milk which can change DNA sequence in babies before weaning. This may open the door to study milk as a new potential method for gene transmission and therapy. A method, that probably overcome many of problems meeting gene therapy as well as a possible cause for evolution in mammalians if we consider cross nursing during milk feeding from other species before weaning.

Introduction

Personal DNA sequence is unique and assumed to be stable all over his or her life span except in some cases of mutation or modification due to endogenous or exogenous factors exposures. Exogenous factors caused mutations include ultraviolet of sunshine, ionizing radiation, mutagenic chemicals and viruses. Endogenous factors include transposons and errors during meiosis process [1, 2, 3].

It is estimated as many as one million individual molecular lesions per cell per day could be found. This constitutes only 0.000165% of the human genome's (approximately 6 billion bases) and some of these lesions may lead to some sort of mutation[4].In addition those DNA sequence changes could also be induced in gene therapy by inserting certain gene or genes using viral vectors mainly or non-viral method to treat certain disease [5].

Anyhow, many problems met gene therapy like short-lived nature of gene therapy and need for multiple rounds of that therapy, immune response for gene or vector as foreigners, problems with viral vectors and malignancy induction [6, 7, 8].

Wet nurse or a foster suckling mother means breastfeeding an infant that is not one's biological offspring's which was well known as a job from ancient Egyptians times to the present [9]. Breast feeding either from biological mother or wet nurse is contraindicated in case of active tuberculosis or aids [10].Shared breast feeding identified as new risk factor in aids[11].So, wet nurse should be healthy, well-nourished , non-smoker and non- alcoholic. She should be also screened for tuberculosis, syphilis, hepatitis-associated antigen, cytomegalovirus, herpes virus, HIV and other infectious agents. Also her biological infant should be healthy, gaining well and free of all infections.

A new relation after foster mother suckling was also found in some holly books that prohibits marriage between the sucker and the suckled and between near relatives of the suckled and the sucker just like real relatives [9].The possible therapeutic potential of factors in human milk was also postulated to treat intestinal immaturity in neonates [12]. Mammary stem cells were also identified in human breast milk [13].

Proposal

Milk from foster mothers may change DNA sequence in babies before weaning and this may open the door for further studies as alternative methods for gene therapy in hereditary diseases in babies before weaning as well as possible factor in mammalians evolution.

Pilot Data:

Here we show significant changes of personal DNA sequence after milk feeding by a selective suckling foster mother which suggests a new potential method for gene transmission and therapy that most probably overcome many problems meeting gene therapy [14, 15].

Methods:

Two groups each consists of three babies exclusively breast feeding , one to two month age, without any type of consanguinity.

Group 1:

It consists of one male and two female babies. Informed Consents were obtained from parents after IRB approval to get four buccal samples for DNA analysis from each baby.

All babies and their mothers were healthy with no possibility *of* infectious diseases.

First buccal swab was taken from each baby for complete DNA scan analysis by decodme genetics, Ltd. Sturlugata 8, IS-101 Reykjavik, Iceland.

Cross nursing was done. Thus, the mother of first baby was asked to give her baby for the mother of second baby for few hours per day to have 3-5 times of suckling per day for a duration of 2 weeks i.e to be as a foster suckling mother for first baby.

The same maneuver was done for second and third baby. It is clear that during that duration of 2 weeks, the rest of feeding for every baby was done by his or her biological mother milk feeding.

For further clarification, the second baby mother became a foster suckling mother for the first baby, the third baby mother became a foster suckling mother for the second baby and the first baby mother became a foster suckling mother for the third baby.

Second buccal swab was taken from each baby for complete DNA scan analysis by the same company.

Another cycle of (cross nursing) for the same duration of 2 weeks and same times of suckling per day by making the second baby mother as a foster suckling mother for third baby, the third baby mother as a foster mother for first baby and the first baby mother as a foster suckling mother for the second baby.

Third buccal swab was taken again from each baby for DNA analysis by the same firm.

After finishing the second cycle, each baby relied upon his or her own biological mother milk feeding and around the age of 6 months additional suitable food may be added before the last samples.

Around the ages of 6 month, fourth buccal swab was taken from each baby only to confirm any possible sustained changes.

Group 2:

It consists of two males and one female. It is the control group.

We had a first buccal swab for DNA analysis from each baby. Then after one month and 6 months of his or her own biological mother exclusively breast feeding, the second DNA buccal swab was taken.

Results

For the first baby, in figure S4 apparent change in genetic sharing of 2nd sample after first foster mother suckling compared to 1stsample before it.

No change could be found in figure S5 in genetic sharing of 3rd sample after second foster mother suckling compared to 1st sample.

Again in figure S6 genetic sharing changes was found in 4th sample at the age of 6 month compared to 1st sample.

For second baby, as shown in figure S1 apparent changes in genetic sharing in 2nd sample after first foster mother suckling compared to 1st sample.

Also changes could be found in figure S2 in genetic sharing of 3rd sample after second foster mother suckling compared to 1stsample.

Also in figure S3 genetic sharing changes was found of 4th sample at the age of 6 month compared to 1st sample.

For the third baby, unfortunately, second sample was of low DNA content unfit for analysis and we couldn't get it again because of the start of the second cycle of foster suckling mothers.

Thus, our data was only for 3rd and 4th samples as in figure S7 apparent changes in genetic sharing of 3rd sample after second foster mother suckling compared to 1st sample.

Also in figure S8 genetic sharing changes were found of 4th sample at the age of 6 month compared to 1st sample. Maximum fragment size was used to see shared chromosome fragments from very recent common ancestors.

Based on a fragment size of 250 kilo base (Kb) - 20 million base (Mb), calculated in the same way as in the Genetic Atlas but with different fragment size and number of comparisons. Genetic sharing of first baby's 2nd, 3rd and 4th sample after foster suckling mothers compared to 1st sample before foster suckling mother was identified as in table no: 1.

The same happened with second baby's 2nd, 3rd and 4th sample after foster suckling mothers compared to 1st sample before foster suckling mother as in table no:2

For third baby only genetic sharing in 3rd and 4th sample after foster suckling mothers compared to 1st sample before foster suckling mother which was identified as in table no: 3.

For control group, genetic sharing of first, second and third control babies' 2nd samples with their1st samples was investigated as in table no: S1.

A comparative study was hold between the first baby genetic sharing changes of mean value of 2nd & 3rd samples after foster mothers suckling and his 1st sample and, mean value of control DNA changes of 2ndsamples (of all control babies) to 1st samples (of all control) . It showed a high significant difference in low DNA sharing (no copy match) using t.test with P value: 0.001 and for medium DNA sharing (only one copy match) P value: 0.002 but with no significant P value for high DNA sharing (two copy match).

A comparative study of the second baby genetic sharing changes of mean value of 2nd & 3rd samples after foster mothers suckling to his 1st sample compared to mean value of control DNA changes of 2nd samples to 1st samples, showed a high significant difference in low DNA sharing (no copy match) P value:0.001 and for medium DNA sharing(only one copy match) P value:0.001 but with no significant P value for high DNA sharing (two copy match).

For the third baby, second sample of low DNA content was unfit for analysis.

A comparative study of the third baby DNA sequence changes of 3rd sample after foster mothers suckling to his 1stsample, compared to mean value of control DNA changes of 2nd samples to 1st samples, showed a high significant difference in low DNA sharing (no copy match) P value:0.001 and also for medium DNA sharing(only one copy match) P value:0.001 but with no significant P value for high DNA sharing (two copy match).

High significant sequence changes were found in only low and medium DNA sharing of first baby's 4th sample (6 month age) compared to 2nd and to 3rd samples of the same baby, p value: 0.001, 0.001, -, 0.001 respectively and also high significant sequence changes occurred in only low and medium DNA sharing of second baby's 4th sample (6 month age) compared to 2nd and to 3rdsamples of the same baby with P: 0.001, 0.049, 0.014, 0.017 respectively.

Again high significant sequence changes took place in only low and medium DNA sharing of third baby 4th sample (6 month age) compared to 3rd sample of the same baby :0.001,0.001 respectively.

Discussion

For my knowledge, this is the first complete scan study of the effect of foster mother milk in human genetics. Decode genetics, Ltd. as a firm analyses about one million Single Nucleotide Polymorphism (SNPs) for complete scan samples.

Many researches used foster pups in mice.

Van der veen R, et al studied the impact of intra- and interstrain cross-fostering on mouse maternal care which demonstrates that both mother strain and pup strain are key determinants of maternal behavior [16].

Another study suggests fostering pup within 24 hours of birth from Helicobacter hepaticas- free mothers to get Helicobacter- free mouse colonies [17].

Improvement in mouse maternal care imposed by replacing biological EL dams with foster CD-1 mothers was sufficient to decrease pup mortality, increase body weight gain (+0.1 g/day) and delay the onset of seizure susceptibility in EL offspring beyond post-natal day 80-90 [18].

The entire mice genome was scanned to search for quantitative trait loci whose effects depend on cross-fostering and detected 10 of such loci. Of the 10 loci, 4 showed imprinting by cross-foster interactions. In most cases, the interaction effect was due to the presence of an effect in either cross-fostered or non-cross-fostered animals.

Genomic imprinting effects may often be modified in mice by the maternal environment and that such interactions can impact key fitness-related traits suggesting a greater plasticity of genomic imprinting than previously assumed [19].

Early-life stress of cross-fostering in mice induced long-lasting emotional abnormalities, which might be possibly related to alterations of serotonin metabolisms [20].

As regard celiac disease, our study showed increase in risk factor in second baby (male) 2nd sample after first foster mother (0.22)compared to his 1st sample before foster mothers (0.17).

Surprisingly, this risk factor returned to 0.17 in his 3rd sample after second foster mother and also in his 4th sample at the age of 6 month suggesting high genome plasticity or repair.

A new study suggest clinical evaluation weighing the pros and cons of nursing male versus female children by mothers with genetically-linked hypersensitivity diseases, such as celiac disease and eczema, or those in regions of the world with endemic DTH-eliciting diseases, such as tuberculosis [21].

Limitations

Some limits are taken into account: number of participating babies in the study is small and a further study must be done to confirm the results. Decodme company where DNA analysis was done is collapsed nowadays and stopped its activities.

Declerations

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Authors’ contributions

Conception and design: K M.E E. Development of methodology: K M.E E. Writing, review, and/or revision of the manuscript: K M.E E, Y K E, E A E & M B S. Study supervision: K M.E E. All authors approved the

final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed Consents were obtained from parents after IRB approval of shefaa City Hospital to get four buccal samples for DNA analysis from each baby.

Consent for publication

Not applicable.

Availability of data and materials

decodme genetics, Ltd. Sturlugata 8, IS-101 Reykjavik, Iceland was the company where all DNA analysis studies were done as a paid service.

Competing interests

no competing interests.

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Tables

Table no: 1

Genetic sharing of first baby 2nd, 3rd and 4th sample with 1st sample

Kilo base (Kb), Million base (Mb), low DNA sharing (no copy match), medium DNA sharing (only one copy match) and high DNA sharing (two copy match)

	First baby 2nd sample compared to 1st sample			First baby 3rd sample compared to 1st sample			First baby 4th sample compared to 1st sample		
Size of fragment	Low DNA sharing	Medium DNA sharing	High DNA sharing	Low DNA sharing	Medium DNA sharing	High DNA sharing	Low DNA sharing	Medium DNA sharing	High DNA sharing
250kb	0.0%	0.2%	99.8%	0.0%	0.0%	100%	0.0%	0.0%	100%
500kb	0.1%	0.5%	99.4%	0.0%	0.0%	100%	0.1%	0.0%	99.9%
1Mb	0.2%	1.6%	98.2%	0.0%	0.0%	100%	0.2%	0.1%	99.7%
2Mb	0.4%	7.1%	92.5%	0.0%	0.1%	99.9%	0.2%	0.2%	99.6%
3Mb	0.0%	0.2%	99.8%	0.0%	0.0%	100%	0.0%	0.0%	100%
5Mb	0.2%	0.1%	99.7%	0.0%	0.0%	100%	0.0%	0.0%	100%
10Mb	1.4%	0.5%	98.1%	0.0%	0.0%	100%	0.2%	0.0%	99.8%
20Mb	3.9%	3.0%	93.1%	0.0%	0.0%	100%	0.9%	1.0%	98.1%

Table no: 2

Genetic sharing of second baby 2nd, 3rd and 4th sample with 1st sample

Kilo base (Kb), Million base (Mb), low DNA sharing (no copy match), medium DNA sharing (only one copy match) and high DNA sharing (two copy match)

	second baby 2nd sample compared to 1st sample			second baby 3rd sample compared to 1st sample			second baby 4th sample compared to 1st sample		
Size of fragment	Low DNA sharing	Medium DNA sharing	High DNA sharing	Low DNA sharing	Medium DNA sharing	High DNA sharing	Low DNA sharing	Medium DNA sharing	High DNA sharing
250kb	0.0%	0.2%	99.8%	0.0%	0.2%	99.8%	0.0%	0.2%	99.8%
500kb	0.0%	0.7%	99.3%	0.0%	0.4%	99.6%	0.1%	0.5%	99.4%
1Mb	0.1%	2.0%	97.9%	0.1%	1.1%	98.8%	0.2%	1.3%	98.5%
2Mb	0.5%	6.7%	92.8%	0.3%	3.4%	96.3%	0.8%	5.1%	94.1%
3Mb	0.1%	0.5%	99.4%	0.0%	0.2%	99.8%	0.0%	0.2%	99.8%
5Mb	0.4%	0.7%	98.9%	0.2%	0.2%	99.6%	0.2%	0.4%	99.4%
10Mb	1.9%	1.3%	96.8%	1.5%	0.2%	98.2%	1.2%	1.7%	97.1%
20Mb	4.2%	5.1%	90.7%	0.7%	3.2%	96.1%	1.7%	4.0%	94.3%

Table no: 3

Genetic sharing of third baby 3rd and 4th sample with 1st sample

Kilo base (Kb), Million base (Mb), low DNA sharing (no copy match), medium DNA sharing (only one copy match) and high DNA sharing (two copy match)

	Third baby 3rd sample compared to 1st sample			Third baby 4th sample compared to 1st sample		
Size of fragment	Low DNA sharing	Medium DNA sharing	High DNA sharing	Low DNA sharing	Medium DNA sharing	High DNA sharing
250kb	0.0%	0.2%	99.8%	0.0%	0.2%	99.8%
500kb	0.0%	0.7%	99.3%	0.1%	0.6%	99.3%
1Mb	0.1%	2.3%	97.6%	0,2%	2.2%	97.6%
2Mb	0.5%	7.4%	92.1%	0.9%	6.4%	92.7%
3Mb	0.1%	0.2%	99.7%	0.0%	0.2%	99.8%
5Mb	0.4%	0.2%	99.4%	0.2%	0.2%	99.6%
10Mb	2.1%	1.3%	96.6%	2.1%	0.5%	97.4%
20Mb	4.7%	8.5%	86.8%	5.9%	4.7%	89.4%

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