CdLS Foundation USA
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To all our member families,

We want to address the issue of Cornelia de Lange syndrome and gene therapy, both to dispel any rumors that have been circulating and to paint a realistic picture of where things stand right now.

Gene therapy is a recent advance in the medical field. It is based on the idea that if a disease or condition is caused by a genetic change in some or all of the cells of the body, then it should be possible to treat that condition by directly altering the genetic makeup of those cells.

Someday, gene therapy may be helpful for a large number of genetic conditions. But right now, the situations in which gene therapy is even conceivable are very limited. Despite recent scientific advances, it is not yet possible to harmlessly edit DNA in hundreds of millions of cells inside a living human being. Currently, technologies carry risks of both over- and under-correcting gene mutations, and might in fact create new, unwanted genetic changes with unknown consequences.

Because of this, gene therapy is currently being developed and tested only for:

1) Conditions that are life-threatening
2) Conditions caused by a mutation that completely eliminates a gene's function, so that restoring any amount of that function would be expected to be beneficial
3) Conditions in which most of the affected individuals carry the *same* mutation
4) Conditions in which restoring gene function to a limited number of cells can be expected to have therapeutic benefit.
5) Conditions in which the risks associated with gene delivery or creating new mutations are outweighed by the expected benefits.

Examples of conditions that meet these criteria include spinal muscular atrophy and sickle cell disease, both of which are the subjects of exciting gene therapy studies that you may have read about in the news.

Unfortunately, most of these criteria do not apply to any form of CdLS. In particular, mutations that cause CdLS generally do not completely eliminate gene function (for example, people all carry two copies of the *NIPBL* gene, and the most common form of CdLS is caused when a mutation occurs in only one of the two copies). Most individuals with CdLS do not carry the same mutations as others—even when the same gene is involved—because most of these mutations are newly-occurring, not inherited from parents. And because CdLS is a developmental syndrome with broad impacts on many organ systems, we do not yet know of any limited group of cells that could be targeted by gene therapy with an expectation of therapeutic benefits.

Over the long term, we can hope that technology will improve to the point where gene therapy can be considered for a wider group of conditions. In the meantime, researchers around the world are working hard to determine what types of therapies—whether involving genes, medications or other interventions—could be both effective and safe for people with CdLS. For ethical reasons, a lot of this work has to be done with animal models, which are expensive to produce and maintain. Scientists associated with the CdLS Foundation have been researching this question worldwide for some time, and are committed to providing therapeutic options to families who are seeking them. Even if gene therapy is not an option now for CdLS, the work these scientists are currently doing can help smooth the way for a time when it may become possible.

We understand that some in the CdLS community may be seeking to raise funds privately for research, including research into gene therapy. The foundation is supportive of all kinds of basic and clinical research to serve the CdLS community, but we are not affiliated with any such private efforts at this time, nor have we authorized the use of the CdLS Foundation logo by them.

Please let your country's CdLS Foundation know if you have any questions or concerns.

Sincerely,

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