proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).

proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).

proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).

proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).

proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).

proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).

proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).

proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).

proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).

proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 133, November 2011
www.proteinspotlight.org

a missing sense

Vivienne Baillie Gerritsen

We are reminded regularly of how fragile life is and how easily the subtle balance of our molecular make-up can be shifted and cause devastating effects. Deafness is one. Deafness can be brought about by a number of incidents. It can occur following an illness or an accident for example. Or it can be congenital. Pendred Syndrome afflicts one out of two thousand human beings and is characterised not only by deafness in both ears but also – though not always – by a swelling in the thyroid gland, otherwise known as goitre. The symptoms of Pendred Syndrome have been known for over a century, but scientists are only just beginning to understand what it is that can leave a human-being deprived of a sense which is so vital. One of the culprits is known as Pendrin – a protein which acts as an ion transporter.

by Judith Scott*

Courtesy of the Creative Growth Art Center
California, USA

Pendred syndrome (PS) was first described in 1896 by an English general practitioner, Dr Vaughan Pendred, who had listened patiently to an Irish mother's account of hearing deficiency which had run through her progeny composed of ten children, all of whom were almost completely deaf and mute. Some of them had also developed goitre, at an early or later age. Following the practitioner's description, further occurrences of goitre coupled with deafness were confirmed, although, with time, it became increasingly obvious that patients afflicted with Pendred Syndrome did not necessarily also suffer from goitre. Thus making the diagnosis of PS a little tricky…

Today, far more is known both on the molecular and the physiological front, and Pendred Syndrome can be diagnosed more easily, and hence faster. The affliction is genetic and causes part of the inner ear of a developing embryo to be malformed. The result is a loss of hearing at birth. The genetic component involved in the syndrome was tracked down in the 1990s, almost exactly a century after Dr Pendred had sent the account of his findings to The Lancet at the end of the 19th century.

The gene involved in PS encodes a transmembrane protein which has been called "pendrin". Pendrin is about 800 amino acids long and is found in the cell membranes of three different tissues: the thyroid gland, the inner ear and the kidney – which would explain the occasional dual occurrence of goitre and deafness when something goes wrong. So far, however, there seems to be no apparent harm caused to kidneys in the event of Pendred Syndrome.

Under normal circumstances, pendrin is a transmembrane ion transporter. When malformed, it could well be that the protein is unsteady, perhaps even wobbly, within a cell's membrane thus causing ion transport to be either faulty or even non-existent. Within the inner ear, pendrin malfunction seems to tamper with endolymph homeostasis – the fluid that flows through part of the inner ear, bathing sensory cells which are so crucial to proper

hearing. This is hardly surprising since pendrin is there to ensure correct ion exchange between the outside and the inside of a cell. In turn, the disturbance of endolymph homeostasis could lead to an abnormal increase in endolymph and the consequent widening of the vestibular aqueducts – which seems to be a characteristic trait of patients suffering from PS.

Regarding the thyroid gland, little is known about how goitre occurs. Nor why. Not all patients develop goitre. Some develop it early on in life, others later, and the severity is variable. So there must be something else which triggers off the swelling of the thyroid gland, with pendrin probably playing only a minor part. As for the kidneys… Well, so far, though pendrin is also found in kidney cells, there has been no report of renal complications linked to deafness.

Until recently, patients suffering from Pendred Syndrome were most probably, and more often than not, misdiagnosed. Looking for deafness coupled with goitre was obviously not a good start – though Dr Pendred's initial observation was astute. Currently, however, PS can be diagnosed by taking a closer look at the structure of the inner ear or, better still, by establishing a patient's genetic profile. And the earlier the diagnosis, the better a child can be looked after. And who knows, perhaps in a few years' time, it will be possible to restore a defective pendrin, and offer spoken words and music to those who have been deprived of them.

---

* Judith Scott was a visual artist who suffered from both congenital deafness and Down's Syndrome.

Cross-references to UniProt

Pendrin, *Homo sapiens* (Human): O43511

References

1. Pearce J.M.S.
   Pendred's Syndrome – Historical Note
   European Neurology 58:189-190(2007)
   PMID: 17622729

2. Reardon W., O'Mahoney C.F., Trembath R., Jan H., Phelps P.D.
   Enlarged vestibular aqueduct: a radiological marker of Pendred syndrome, and mutation of the PDS gene
   Quarterly Journal of Medicine 93:99-104(2000)
   PMID: 10700480

3. Dossena S., Rodighiero S., Vezzoli V., Nofziger C., Salvioni E., Boccazzi M., Grabmayer E., Bottà G., Meyer G., Fugazzola L., Beck-Peccoz P., Paulmichl M.
   Functional characterization of wild-type and mutated pendrin (SLC26A4), the anion transporter involved in Pendred syndrome
   Journal of Molecular Endocrinology 43:93-103(2009)
   PMID: 19608655

Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).