



# Irish giants: from myth to medicine

Wouter W. de Herder<sup>1</sup> · Paul Benjamin Loughrey<sup>2</sup> · Márta Korbonits<sup>3</sup> · Adrian F. Daly<sup>4</sup>

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## Abstract

The archetype of the ‘Irish giant’ in folklore appears to be rooted in historical individuals afflicted by pituitary gigantism. This review compiles and critically assesses the veracity of historical accounts, primarily from the late 17th to the early 20th century, for a group of individuals with gigantism that had Irish origins. Clinical and, in some cases, osteological data (e.g., Charles Byrne, Cornelius Magrath, and Patrick Cotter) confirm a diagnosis of pituitary gigantism, a rare disease that is caused by excess growth hormone secretion from a pituitary adenoma. In the pre-scientific era, the effects of the unopposed hormone excess resulted in extreme tall stature, debilitating morbidity, and usually premature death. This aligns with our modern understanding of the potential severity of hormonal excess and tumour growth in pituitary gigantism. The high concentration of cases in Ulster is explained by a founder germline pathogenic variant (c.910 C>T, p.(R304\*)) in the *AIP* gene, that was identified in multiple contemporary families, later in the skeleton of Charles Byrne and most recently, among the Irish diaspora. Estimated to have arisen around 2500 years ago, this variant established a direct medical explanation for a regional phenomenon. In this review we provide a detailed compilation of historical Irish giants and discuss the evidence linking myth and folklore to the modern medical reality of pituitary gigantism as a rare, severe genetic disease.

**Keywords** Gigantism · Ireland · Pituitary · Giant · Mythology · History · Genetics · AIP · Founder · Hotspot

## Introduction

Folklore across cultures makes use of standard archetypes as the basis for myths, legends and fables. Among the most pervasive of these standard figures are individuals with tall and short stature. Their size sets them apart, and can imbue them with otherworldly, magical or super-human characteristics [1]. Irish folklore has well known examples

of short fairy folk like leprechauns, while some legendary figures are described as having gigantic characteristics. Fionn MacCumhaill, perhaps the most famous warrior in Irish mythology, began as a normal-sized boy and man, albeit one who performed extraordinary feats of valour. In later stories Fionn is described as having superhuman size and strength, which he used to form landscape features like the volcanic Giant’s Causeway in County Antrim and Fingal’s cave on the Scottish Coast. Fionn was a giant and a warrior, and in one legend he battled the Scottish giant Benandoner, scooping up rock and earth to form Lough Neagh; Fionn missed his throw and the rocks became the Isle of Man. An enormous dolmen in Proleek in County Louth was also linked to an Irish-Scottish giant rivalry, this time between Fionn and Para Beag Mac Seoidin; the dolmen is known as the Giant’s Load [2, 3]. Further afield, the giantess Grana (Grania or Gráinne) dwelt on the Rock of Carrigogunnell in County Limerick [4]. Stories of such giants, warrior-like or magical in nature, are, however, very common in other mythologies, and are not particularly unique to Irish stories. How did these universal tall figures arise? As they often take a human form, we could

✉ Wouter W. de Herder  
w.w.deherder@erasmusmc.nl

<sup>1</sup> Department of Internal Medicine, Sector of Endocrinology, Erasmus Medical Center, Rotterdam  
3015 GD, The Netherlands

<sup>2</sup> Department of Endocrinology, Beaumont Hospital, Dublin, Ireland

<sup>3</sup> Department of Endocrinology, William Harvey Research Institute, Queen Mary University of London, London, UK

<sup>4</sup> Department of Endocrinology, Centre Hospitalier Universitaire de Liège, Liège Université, Domaine Universitaire Sart-Tilman, Liège 4000, Belgium

speculate that they were inspired by real life encounters with historical tall people.

Spanning a long gap from the mythology of the past, accounts of giants in Ireland first begin to appear in the press toward the end of the 17th century. These reports, a mixture of medical curiosities, speculation and publicity mainly concern people afflicted by gigantism that displayed themselves in public. The spectacle of an “Irish Giant” was also tinged by negative socio-political attitudes that emerged in ethnology to support a view of a distinct but primitive Celtic Irish “race”. As noted in Radian et al., British ethnologist, James Cowles Prichard (1786–1848) wrote: “*In Ireland men of uncommon stature are often seen, and even a gigantic form and stature occur there much more frequently than in this island....We can hardly avoid the conclusion, that there must be some peculiarity in Ireland which gives rise to these phaenomena*” [5, 6]. Was there another, more scientific factor that could have explained why giants seemed to be more common in Ireland?

Tall stature is a multifactorial condition that is generally defined as a height greater than two standard deviations above the population mean for age and sex [7]. Among the many causes of isolated and syndromic tall stature, pituitary gigantism is generally the most extreme form [8, 9]. This rare condition that lies at the severe end of the disease spectrum of acromegaly, is usually caused by a growth hormone (GH)-secreting pituitary adenoma [9]. Whereas acromegaly typically becomes apparent in the fourth/fifth decades of life and affects men and women nearly equally, pituitary gigantism, in contrast, predominantly affects males (60–65%) and begins in childhood and adolescence before the fusion of growth plates [8–10]. Pituitary gigantism patients have a far higher rate of germline/inherited genetic causes than those with adult-onset acromegaly (50% versus < 1–2% respectively) [9, 11, 12]. The most frequent genetic cause of pituitary gigantism is a pathogenic germline variant in the *aryl hydrocarbon receptor interacting-protein (AIP)* gene, which can lead to early presentation with large pituitary adenomas (GH- and/or prolactin-secreting) that often occur in the familial setting (a condition called familial isolated pituitary adenomas (FIPA)) [13]. Clustering of cases of historical gigantism in the North of Ireland, and the availability of skeletal remains of one such giant, Charles Byrne, led to the identification of a founder *AIP* gene variant in Ulster [14]. The founder of this variant may have come from the distant past (approx. 2500 years ago) and, theoretically at least, could have acted as an inspiration for legends and folklore. This discovery has more than historical importance as it led to the identification of this *AIP* variant among many current patients in the North of Ireland and recently among the extensive Irish diaspora in the United States [6, 15, 16].

In this review we revisit historical accounts of giants from and linked to Ireland and assess the veracity and characteristics of descriptions made in various media, including the customary exaggeration of heights for advertising purposes. From the geographical spread of these individuals the role of *AIP* in the pathophysiology of those originating in or with direct familial links to Ulster can be seen.

## Historical giants born in Ireland

### Leinster

#### Edmond Malone 1665 –?

Edmond (Edmund) Malone (Melloon) was born at Portlister, County Meath in 1665. In 1682, the Irish physician, Sir Thomas Molyneux (1661–1733) measured the 17-year-old Malone in Dublin as being “*7 feet 7 inches (2.31 m) tall in his bare feet*” [17]. The naturalist and antiquarian Robert Plot (1640–1696) who became the first keeper of the Ashmolean Museum saw him in Oxford in 1684 and concluded that his height was 7 feet 6 inches (2.28 m) [18].

The same year Malone appeared at Court before King Charles II. In his advertisements it was stated that the amazed King had walked under Malone’s outstretched arm:

*“The Gyant; or the Miracle of Nature. Being that so much-admired young man, aged nineteen years last June, 1684. Born in Ireland, of such a prodigious height and bigness, and every way proportionable, the like hath not been seen since the memory of man: he hath been several times shown at court, and his majesty was pleased to walk under his arm, and he is grown very much since, he now reaches ten feet and a half, fathoms near eight feet, spans fifteen inches; and is believed to be as big as one of the giants in Guildhall. He is to be seen at the sign of the Catherine Wheell [sic] in Southwark fair. Vivat Rex”.*

Two legendary giants, Gog and Magog, are associated with the Guildhall in London and at that time consisted of two effigies made of wicker and plasterboard that were later replaced by carved wooden giants [3]. The Catherine Wheel Inn was a famous hostelry, while the fair at Southwark took place near the Church of St George the Martyr in south London [19]. The date and place of death of Edmond Malone are unknown.

#### James Kirkland (Early 18th century)

James Kirkland was a native of Ballygar, Ardagh, County Longford. He was one of the tallest soldiers recruited by Friedrich Wilhelm I, King of Prussia (Friedrich von

Preußen, 1688–1740) for his regiment of tall soldiers often called the “Potsdam Giants”, or “Lange Kerls”. A portrait by Johann Christof Merck dating from 1718, possibly showing Kirkland as a Grenadier of the Potsdam Giants, is in the collection of the *Deutsches Historisches Museum* in Berlin, Germany (Fig. 1a). His height is described at the bottom of the painting as “6 Fuss 8 Zoll”; from Prussian measurements this converts to 2.17 m., or 7 feet 1 inches.

Friedrich Wilhelm I had what he himself called a “weakness for tall soldiers” [20]. A team scouted Europe on his behalf for tall men. Kaspar Wilhelm von Borcke (1704–1747) was a Prussian diplomat in London who spotted Kirkland. He closed a deal on behalf of Friedrich Wilhelm I that he would receive £1,000 and that Kirkland would obtain £60 as 3 years’ wages to come to Germany with the extraordinary proviso of “on condition of his giving up his person”. By the time of Friedrich Wilhelm’s death, the reputation of Kirkland and the “Lange Kerl” regiment had spread throughout Europe. It is unknown what became of Kirkland [21].

### James Clancy 1812 –?

James Clancy was born in 1812 near Arklow, County Wicklow. His final height was 7 feet 2 inches (2.18 m) and his

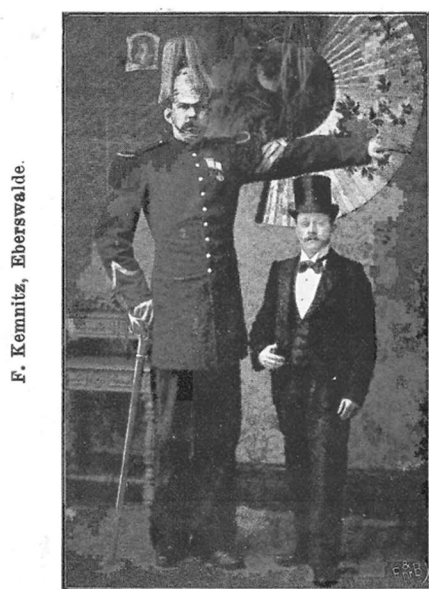
parents were normally sized. In 1832–33 he appeared at the Camberwell and Bartholomew Fairs in England [22]. In 1838, he emigrated to the United States, where he appeared as “The Irish Giant, James O’Clancey” in the company of Miss. S.G. Shore “the Albino Lady”. The couple appeared between 1838 and 1840 in New York, South Carolina, Virginia and Washington DC. In 1843, he was appearing at Worcester, Massachusetts together with Charles Sherwood Stratton (1838–1883, better known by his stage name “General Tom Thumb”, a famous American with extreme short stature (1.02 m., 3 feet 4 inches). In 1843, the *Saturday Morning Transcript* noted that O’Clancey (sic.) was one of the “tallest, well-proportioned men now living,” and emphasised his “manly form...wit...and frank and open countenance”. His date of death is unknown.

### James Patrick Tolley c. 1839 –?

James Patrick Tolley (also referred to as James Patrick Folly and James Patrick Fahy) was born in County Carlow in about 1839. He was 7 feet 5 inches (2.26 m) tall and exhibited himself at fairs in the south of Belgium and north of France, after which he was expelled to England, where he was in trouble with the law by 1887. He may have spent



a



F. Kemnitz, Eberswalde.

Irlands grösster Riese T. Dalroy.

b



c

**Fig. 1** (a) James Kirkland, early 18th century, pictured as “Lange Kerl”, Grenadier of the Potsdam Giants. Portrait by Johann Christof Merck dating from 1718. Collection of the “Deutsches Historisches Museum” in Berlin, Germany. Global Public Domain Content available on Wikimedia commons, <https://commons.wikimedia.org/>. (b) Thomas Dalroy, late 19th century-early 20th century. Postcard printed

by F. Kemnitz, Eberswalde, Brandenburg, Germany. Collection of W. W. de Herder. (c) Cornelius Magrath (1760–1806) by Pietro Longhi (1701–1785) “Il gigante Magrat” (1760), oil on canvas. Ca’ Rezzonico Museum in Venice, Italy showing. Global Public Domain Content available on <https://commons.wikimedia.org/>

significant time in America, and the date and manner of his death are unknown.

### Thomas Dalroy (Late 19th century-early 20th century)

Thomas Dalroy from Kildare was claimed to be 7 feet 6.5 inches (2.30 m) tall. According to a newspaper article in the Australian newspaper *Riverina Times* of 31 January 1901, he was serving as a Sergeant of the Royal Dragoons in South Africa. He had also served in several Egyptian campaigns. It was mentioned that he “*came of a race of giants, his father being over 7 feet tall*” (Fig. 1b). He was touring England (London Aquarium) and mainland Europe and appeared in Liège, Belgium in 1886.

## Munster

### Cornelius Magrath 1736–1760

Cornelius Magrath was born near Silvermines, County Tipperary on 10th March 1736. His parents and siblings were of normal height. Between the ages of 15 and 16 he reputedly grew from 5 feet (1.52 m) to 6 feet 8¾ inches (2.05 m) in height. In 1752, at the age of 16, he came to Youghal, County Cork for saltwater baths to alleviate the violent pains in his limbs, which were most probably caused by his rapid growth [3, 23, 24]. While in Cork, George Berkeley (1685–1753), the Church of Ireland Bishop of Cloyne, took care of him for a few months, possibly administering his favoured tar-water treatment [3]. Meanwhile, Magrath was followed by large crowds of curious people, and he was persuaded to exhibit himself for money. He moved to London, England and became well known. As noted in the press in 1753:

*“Just arrived in this city, from Ireland, the youth, mentioned lately in the newspapers, as the most extraordinary production in nature. He is allowed by the nobility and gentry, who daily resort to see him, to have the most stupendous and gigantic form (altho’ a boy), and is the only representation in the world of the ancient and magnificent giants of that kingdom. He is seven feet three inches in height, without shoes. His wrist measures a quarter of a yard and an inch. He greatly surpasses Cajanus the Swede, in the just proportions of his limbs; and is the truest and best proportioned figure ever seen. He was sixteen years of age the 10th of last March and is to be seen at the Peacock, at Charing Cross, from eight in the morning, till ten at night”.*

The “Cajanus” mentioned refers to Daniel Cajanus (1702–1749) who was a Finn with gigantism measuring 7 feet 4½

inches (2.25 m). Magrath later toured several European cities. In 1757, the Italian physician-anatomist Giovanni Bianchi (1693–1775 - also known as Jano Planco) having encountered Magrath in Rimini, Italy, wrote a medical report [25]. In 1760 an oil on canvas painting was completed by the Venetian painter Pietro Longhi (1701–1785); entitled “Il Gigante Magrat” and is displayed in the Ca’ Rezzonico Museum in Venice, Italy (Fig. 1c). In Flanders Magrath caught a fever and was forced to return to Dublin where he arrived in March 1760.

It was reported that: “*his complexion was miserably pale and sallow; his pulses very quick at times for a man of his extraordinary height; and his legs were swollen*”.

It was believed that he suffered from phthisis (pulmonary tuberculosis), while the description of his condition also suggests heart failure. On 16 May 1760 he succumbed. His final height was between 7 feet 5 inches (2.26 m) and 7 feet 8 inches (2.34 m). His body was dissected at Trinity College Dublin, but the skeleton of Magrath was not extensively studied until 1890. At that time Daniel Cunningham, Professor of Anatomy at Trinity College Dublin confirmed that Magrath had suffered from acromegaly and documented an enlarged pituitary fossa (length 38 mm, depth 28 mm), which must have been caused by a pituitary macroadenoma [24, 26]. On the basis of Cunningham’s report, the renowned ophthalmologist Sir Henry Swanzy (1843–1913) postulated that Magrath should have suffered from visual defects and loss of visual acuity caused by an invasive large pituitary macroadenoma [27]. Interestingly, a DNA sample from Magrath’s skeleton was found to be negative for pathogenic *AIP* variants [6].

### Patrick Cotter 1760–1806

Patrick Cotter was born in 1760 in Kinsale, County Cork to parents that were of average height. He reportedly reached a final height of 8 feet 1 inches (2.46 m). Already at a young age Cotter was hired by a showman to appear in England at fairs and shows for a fee of £50 for 3 years that was paid to his father (12).

While visiting Northampton at the age of 17, he was described by a hairdresser as follows:

*“his features were regularly formed, his countenance remarkably healthful, and his standing position erect and commanding. The mildness of his temper was conspicuous and he possessed intelligence of a superior order to that usually discovered by the individuals of the trade to which he was apprenticed - a bricklayer. His stature, eight feet seven inches and three-fourths, did not make him appear disproportionate; in every aspect he was a well-made man”* [3, 23, 28].

With the aid of a benefactor, Cotter – then aged 18 - managed to terminate this abusive contract in Bristol, and from that time he appeared for his own profit [3]. He used his stage name *O'Brien/Patrick O'Brien* for theatres and fairs and was also known as the “Bristol Giant” and the “Irish Giant”. The name “O'Brien” was used for advertising purposes to allude to descent from High King of Ireland, Brian Boru (fancifully a “giant”).

After Charles Byrne's death in 1783 it was reported that: *“The vast concourse of Nobility and Gentry, who saw Mr O'Brien (= Patrick Cotter) at No. 30 St. James's Street, on Friday last, hath greatly excited public curiosity. The wide difference between this gentleman's behaviour and the late Mr Burn's (= Byrne) cannot fail to insure him success; for while his uncommon stature fills the mind with wonder, his ease and affability commands respect”* [3].

The effects of his underlying disease took their toll. By 1804, the description of Cotter had changed completely; William Blair (1766–1822), surgeon at the Lock Hospital in London noted:

*“he was of very extraordinary stature, but not well-formed. As he would not suffer a minute examination to be made of his person, it is impossible to give any other than a very slight description of him. He declined the proposal of walking across the room and I believe was afraid of discovering his extreme imbecility. He had the general aspect of a weak and unreflecting person....”*,

*“His legs appeared swollen, misshapen and I thought dropsical....”, “He certainly had a greater redundancy of bone than of muscle, and gave me the impression of a huge, overgrown, sickly boy, his voice being rather feeble as well as his bodily energies, and his age appearing under that which he affirmed”*.

*“The state of his pulse agreed with the general appearance of his person, viz. feeble, languid and slow in its motions”* [29].

During his life it was noted that he suffered from severe progressive joint problems [3, 28, 30]. The initial part of Blair's account is clearly coloured by his annoyance at Cotter's unwillingness to undergo detailed examination [29]. However, the comments do suggest chronic acromegalic characteristics, such as, arthropathy, hypopituitarism and, like the reports on Cornelius Magrath above, signs of heart failure. Patrick Cotter died in Bristol, England in 1806: *“having fallen a sacrifice of a disease of the lungs combined with an affection of the liver”* [30].

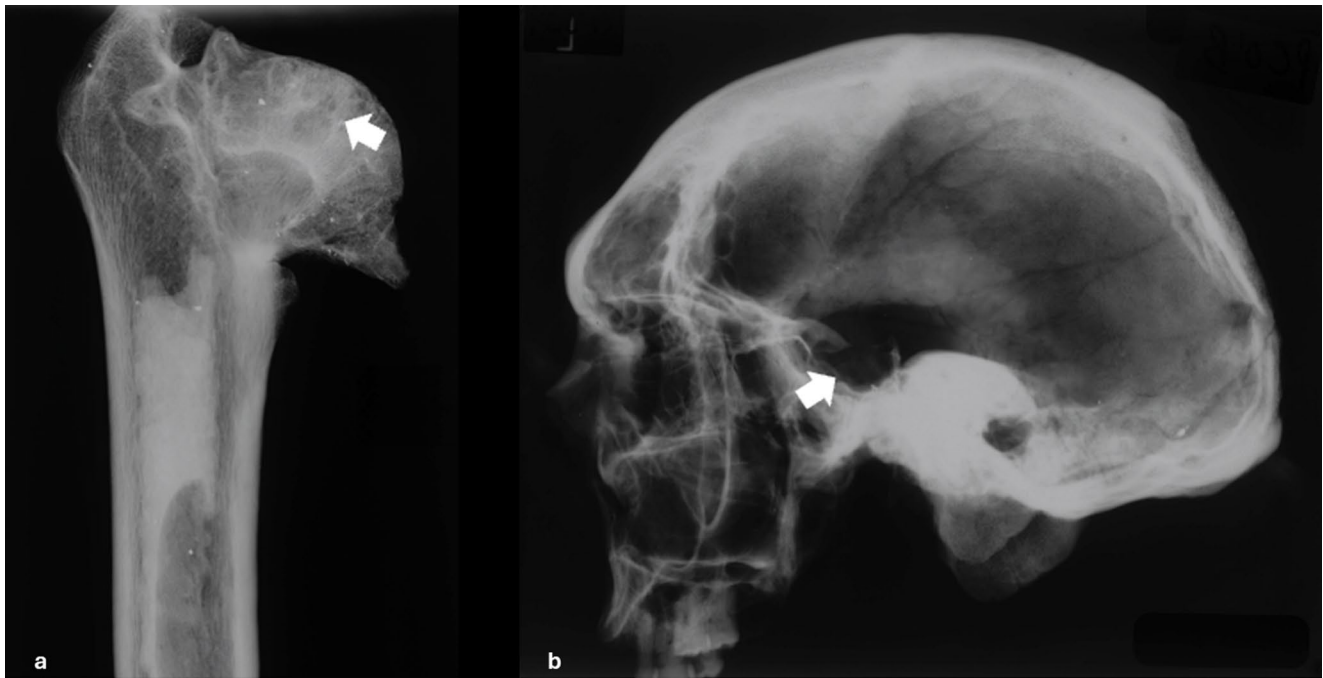
In his will, Cotter had requested that his body be buried in 12 feet (3.70 m) of solid rock to prevent body snatching [31]. However, a century after his death, construction workers at the site of the old Catholic church in Bristol exhumed his coffin. His remains were examined, measured and photographed on site by the English anatomist Edward Fawcett (1867–1942) and reburied thereafter [28]. Fawcett noted that.

*“the skull was in good condition and was especially remarkable for the enormous development of the face”. “It was quite easy to feel from the foramen magnum that the pituitary fossa of the skull was enormously enlarged”* [28].

In 1972, Cotter's remains were re-excavated during the renovation of the church and examined again by Graham Frankcom and Jonathan Musgrave, and it was again concluded that Cotter had suffered from acromegalic gigantism and that, while alive, he measured approximately 2.46 m (8 feet 1 inch) [30]. X-rays taken at the time demonstrate well some of the abovementioned pathological features of pituitary gigantism. As shown in Fig. 2a, his right femoral head was severely damaged. As acromegalic gigantism predisposes to slipped capital femoral epiphysis, it is possible that he suffered from this condition as a teenager [32–34]. Untreated slipped capital femoral epiphysis severely distorts the hip joint, often progressing into chronic pain, debilitating osteoarthritis, and permanent joint damage. Without surgical stabilisation, the femoral head continues to slip, significantly accelerating physical decline and the ability to walk. These findings correspond with the fact that he was often depicted as leaning on a door with his right arm and was reluctant to walk through a room. Skull x-rays clearly show the enlarged sella turcica typical of the effects of an expansive pituitary macroadenoma (Fig. 2b.) Cotter's remains were excavated again as the church was redeveloped for housing in 1986 and are thought to have been cremated [6].

### Eliza Simpson 1828 –?

Eliza Simpson was born in Bantry, County Cork in 1828. She was billed at 8 feet 0 inches (2.44 m) in height but might have been between 7 feet 0 inches (2.13 m) and 7 feet 2 inches (2.18 m) She was also known as the “Scotch Giantess” and the “Quaker Giantess”. On 4 March 1849 she “married” the 7 feet 6 inches (2.286 m) tall Englishman Robert Hales, who was known as the “Quaker giant”. Robert Hales was born on 2 May 1820 in Somerton, Great Yarmouth, Norfolk. Both Eliza Simpson and Robert Hales at that time worked for the American Museum of Phineas Taylor Barnum (1810–1891), the American showman,



**Fig. 2** (a) Radiograph of the right hip of Patrick Cotter following an excavation in 1972. Severe deformity of the femoral head (arrow) and neck due to osteoarthritis is evident, which may have been due to a slipped capital femoral epiphysis. (b) Lateral skull x-ray shows exten-

sive pathological changes with frontal expansion due to hyperostosis, prominent frontal and maxillary sinuses and a greatly expanded pituitary fossa (arrow). Radiographs by J.H. Musgrave, courtesy of Prof. Márta Korbonits

businessman, and politician, and co-founder of the Barnum & Bailey Circus. (Fig. 3a). This “marriage” was considered to have been a publicity stunt by P.T. Barnum. In 1851, Robert Hales returned to England without Eliza Simpson and in 1852 married Maria Charlotte Webb. Robert Hales died on 22 November 1863 in Great Yarmouth, Norfolk, England. It is unknown where and when Eliza Simpson died.

#### (James) Hugh Murphy Jr 1842–1875

(James) Hugh Murphy Jr. was born in 1842 in Waterford and died in 1875 in Baltimore, Maryland, USA. He was known as the “Colossal Irish Giant” and the “Baltimore Giant” (Fig. 3b). He was hired around 1860 by P.T. Barnum. Barnum billed Murphy being over 8 feet tall, but his real height was around 7 feet 1.5 inches (2.17 m) [3, 35].

#### Patrick O’Connor 1881–1922

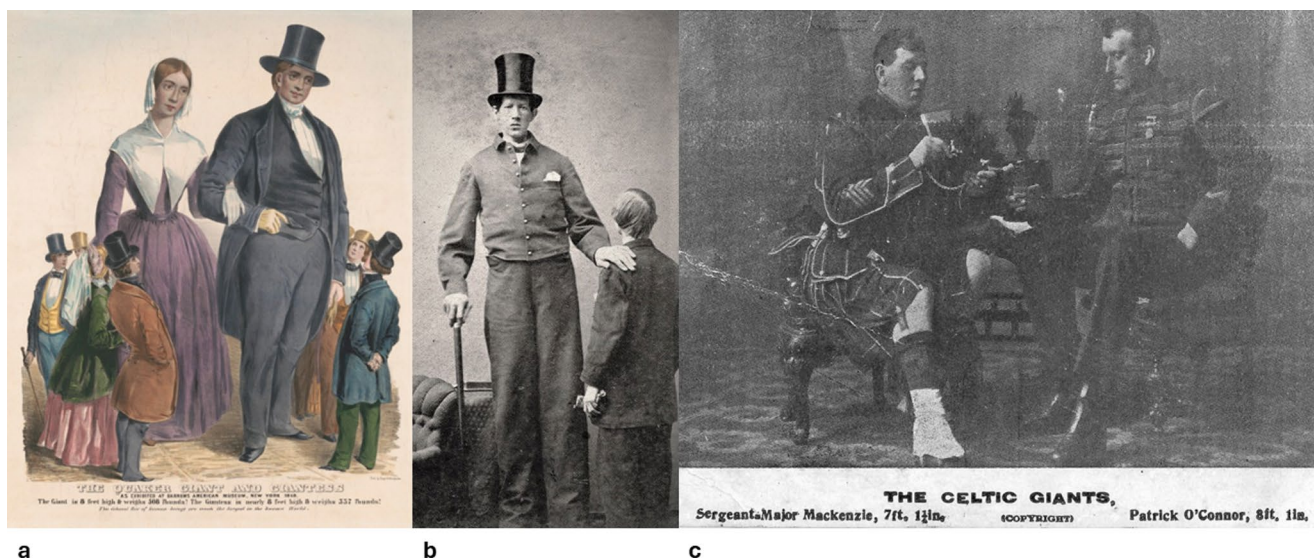
Born in 1881 in County Tipperary, Patrick O’Connor was 7 feet 4 inches (2.23 m) tall. He claimed that he had once been a private soldier, fighting in Sudan, Afghanistan and South Africa (Fig. 3c). Patrick O’Connor stayed in London from 1909 to 1911 and several postcards showing him in different forms of attire were issued during this period [36]. In July 1911, he moved to Australia and was advertised as being 8 feet 3 inches (2.51 m) tall. Thereafter, he travelled

throughout Australia, using “the Tipperary Giant” as his stage name. In the Tasmanian newspaper, *The Mercury* of 17 January 1912, it is mentioned that he was one of twin brothers and that his brother also had gigantism, measuring 7 feet 4 inches (2.24 m).

Initially he was reasonably successful, but later fell on hard times, and was imprisoned. When he was released from prison, O’Connor joined the Australian Army. A photograph in the Sydney Mail from 21 June 1916 shows him towering over two other recruits at the Goulburn army camp. The “Tallest Man in the Australian Army” successfully completed his training and went to the UK but did not see active service due to his height and joint pains. Before he returned to Australia in November 1917, he served as a guardsman at the High Commissioner’s office in London for 18 weeks to advertise Australia. He died in Lidcombe just outside Sydney in August 1922 and was buried at Rookwood, Sydney, New South Wales, Australia.

#### Jim Cully 1922–1981

Jim Cully was born in Tipperary on 1 January 1922 to James Cully and Mary Ryan and had family links to the North of Ireland. His maximum reported height was 7 feet 2 inches (2.18 m). He started out as weightlifter on Irish fairgrounds and between 1942 and 1948 “Tiny” Cully alias “the Tipperary Tower” would enjoy a short, and ultimately



**Fig. 3** (a) Robert Hales & Eliza Simpson standing among a group of onlookers at Phineas Taylor Barnum's American Museum, New York. Hand coloured lithograph printed by Nagel & Weingärtner, New York, NY, USA c.1849. Copy in the collection W.W. de Herder. Global Public Domain Content available on Wikimedia commons, <https://commons.wikimedia.org/>. (b) (James) Hugh Murphy Jr (1842–1875), alias the “Colossal Irish Giant” or the “Baltimore Giant” (and an unknown

man), aged 18 years appearing at Barnum's Museum, New York, USA. From an 1852 picture in the collection of W. W. de Herder. (c) Patrick O'Connor 1881–1922 and Roderick Bain M(a)ckenzie 1867–1939, who was born in Canada and had Scottish ancestors and whose height was 7 feet 2.5 inches (ca. 2.20 m), early 20th century. Postcard in the collection of W. W. de Herder

unsuccessful professional boxing career. He won the Irish National Heavyweight Title in 1942, then fought six boxing matches (four in Ireland and two in the US) of which he won three and lost three. During his sporting career, he was frequently referred to as the “Giant of Tipperary” or the “Goliath of Ireland”. Cully also enjoyed some popularity as a wrestler named “The Gargantuan Gael” after he hung up his gloves. He died at the age of 59 in 1981. Jim Cully's family are known to be heterozygous for the *AIP* p.(R304\*) variant (see below) and in a newspaper interview with the St. Petersburg Times on April 19, 1948, Cully stated that his grandfather was also a giant, measuring seven feet four inches tall [6].

## Connaught

### Michael Grealish 1892 –?

Michael Grealish was born in Bohola, County Mayo on 20 May 1892 and emigrated to Canada at the age of 14 when he was 6 feet 2 inches (1.88 m) tall. In May 1916, several US and Canadian newspapers reported that he measured 7 feet 2 inches (2.18 m) in height and had a reach of 92–93 inches (2.33–2.36 m) when he was groomed to become a boxer and fight the then world champion Jess Willard (1881–1968) [6]. However, there is no record of a professional boxing match between Michael Grealish and Jess Willard, and it is not known what became of Grealish.

## Ulster

### Mary Murphy 1673–1701

Mary Murphy was born in Portrush, County Antrim around 1670–1673. She married a French sea captain who was passing through the port, and they started touring the countryside appearing as an attraction at fairs (Fig. 4a). She danced an Irish folkdance and sang for King William and Queen Mary who paid her one guinea. She was last seen in 1701 appearing at a fair outside Paris, but by this time she had been abandoned by her husband. It is evident that she died in France, but the date, place and cause of her death are unknown [3].

Evidence of her rather tragic story comes from a manuscript dating from 1730 in which James Paris du Plessis mentions that he saw in London in 1696:

*“a giantess who was seven feet (2.13 m) high without her shoes, who was born in the Isle of Portrush, not far from the wonderful Causeway in the most northern part of Ireland.”*

In 1701, he saw her again at a fair in Montpellier, France:

*“I not knowing she was the same I had seen five years before in London, and though I was something disguised by wearing a periwig, she remembered me very well and told me where she had seen me” [37].*



**Fig. 4** (a) Mary Murphy 1673 -c.1701. From James Paris: England; early 18th century. The caption reads: "Drawing of a woman from Portrush, Ireland, 'seven feet high'; seen by James Paris in London in 1696, and in Montpellier in 1701". Global Public Domain Content British Library, <https://wellcomecollection.org/b>. Etching from 1803 by the Scottish caricaturist and engraver John Kay (1742–1826) showing Patrick Cotter (O'Brien), the Irish Giant (1760–1806) and William Ranken. Caption reads: "Mr. O'Brien the Irish giant the tallest man in the known world being near nine feet high" (53). Copy in the collection of W. W. de Herder, also Global Public Domain Content available on <https://commons.wikimedia.org>. National Portrait Gallery, London, UK., or <https://wellcomecollection.org/>. (b) Caricature etching by the Scottish caricaturist and engraver John Kay (1742–1826): "Three giants with a group of spectators", showing Charles Byrne (O'Brien) (1761–1783) flanked by the Knipe twin brothers (c1761–) and among the spectators are: Andrew Bell (in front at the left) William Richardson (on the left behind); Lord Monboddo (head in the background); James Burnett; Bailie John Kyd (at the right); a lady and a short male individual (53). Copy in the collection of W. W. de Herder, also available on <https://commons.wikimedia.org/> – National Portrait Gallery, London, UK, or <https://wellcomecollection.org/>

### Thomas Fanton 1745 -?1782

Thomas Fanton was described in newspapers of the time as the "Hibernian Giant", although there is some uncertainty if he appeared under different stage names and he may have been confused with other "Irish Giants" appearing during that period [38]. Fanton's height was reported in the range 8 feet to 8 feet 3 inches and his arrival in London preceded Charles Byrne (below) by more than 9 months. He was described by the artist Burt as appearing with two individuals with dwarfism from Wales and England [39]. Fanton was reportedly born in Omagh, County Tyrone in the geographical AIP hotspot.

### Charles Byrne 1761–1783

Charles Byrne was born in 1761 in Littlebridge, County Derry. His Irish father and (possibly) Scottish mother were of normal stature and he was reputedly not an unusually large baby. During childhood he "grew like a cornstalk", soon towering over the adults of the village. He reached a final height of 7 feet 7 inches (2.31 m) [3, 20] (Fig. 4b). As a teenager, Charles Byrne appeared at local fairs and markets, represented by an entrepreneurial manager named Joe

Vance. Convinced that he could attract much larger crowds and thus more money, Vance decided to tour England. After his arrival in London in April 1782, Byrne was advertised as measuring 8 feet 2 inches (2.49 m). Byrne started appearing at several London addresses, usually six days a week. Rumours of Byrne's financial success also inspired others to try their luck in London like the "Gigantic Twin Brothers" Knipe (see below), who were from the same region as Byrne and claimed kinship with him (Fig. 4c) [3, 20].

Fame and wealth followed, but his health diminished rapidly and he was claimed to have a fear of having his body stolen for dissection by anatomists. After his death, his body was to be sealed in a lead coffin and to be watched day and night by his loyal friends until it could be sunk at sea. On 1 June 1783, Charles Byrne died in his apartment at the age of 22. A newspaper described the aftermath as follows:

*"The whole tribe of surgeons put in a claim for the poor departed Irish Giant, and surrounded his house just as Greenland harpooners would an enormous whale. One of them has gone so far as to have a niche made for himself in the giant's coffin, in order to his being ready at hand, on the witching time of night, when church-yards yawn".* From another newspaper dated

June 13th, 1783: “*Since the death of the Irish Giant, there have been more physical consultations held, than ever were convened to keep Harry the Eighth in existence. The object of these Aesculapian deliberations is to get the poor departed giant into their possession; for which purpose they wander after his remains from place to place, and mutter more fee, faw, fums than ever were breathed by the whole gigantic race, when they attempted to scale heaven and dethrone Jupiter.*”

While the precise details remain unclear, the remains of Charles Byrne came into the possession of the leading surgeon and anatomist, Dr. John Hunter [3, 20, 31]. Hunter himself never explicitly described the scheme to obtain the remains. To escape potential scrutiny, the skeleton of Charles Byrne was put on display in Hunter’s Museum only 4 years later, after the public’s interest had waned [20, 31, 40]. An oil on canvas portrait of John Hunter in 1813 by John Jackson (1778–1831), based on a work of 1786 by Sir Joshua Reynolds (1723–1792), depicts John Hunter seated at his writing table surrounded by specimens from his collection and the shin bones and feet of the skeleton of Charles Byrne are visible in the top right-hand corner. Byrne’s skeleton is part of the Hunterian Collection at the Royal College of Surgeons in London, UK.

John Hunter could also have been the first to describe pituitary enlargement in gigantism/acromegaly, but he did not explore the skull of Charles Byrne. As the legendary neurosurgeon Harvey Cushing observed, “*his passion as a collector exceeded his thirst for knowledge*” [41–43]. In 1909, Cushing together with the curator of the Hunterian Museum, Sir Arthur Keith, opened the skull and demonstrated that the sellar floor was enlarged measuring 21 × 24 mm and was 11 mm deep [44–46]. Although Charles Byrne was 22 years old when he died, radiographic images of his wrist bones showed that the epiphyses were not yet fused. In 1980, the Swiss neurosurgeon Alex M. Landolt and paediatric endocrinologist Milo Zachmann estimated his “bone age” to be only about 17 years, indicating that he was still growing at the time of death and implying that Charles Byrne had hypogonadism at a late age [47].

DNA was extracted from the teeth of Charles Byrne and identified a germline pathogenic variant (c.910 C > T, p.(R304\*)) in the *AIP* gene [14]. The exploration of the origins and extent of this *AIP* pathogenic variant in historic and contemporary families from or with roots in mid-Ulster are discussed below.

### Knipe Twins c.1761 –?

The Knipe Brothers from Magherafelt, County Derry, were recorded as being 7 feet 2 inches (2.18 m) tall. At the age of 24, they toured London as ‘the Gigantic Irish Twins’ in

1784–1785 (Fig. 4c) [3]. Charles Byrne was purportedly their cousin.

The twin Knipe brothers issued the following handbill:

*“Irish Giants. The most surprising gigantic twin brothers are just arrived in this metropolis, and to be seen at the Silk-dyer’s, No. 2 Spring-gardens, Charing Cross. These wonderful Irish giants are but twenty-four years of age, and measure very near eight feet high. These extraordinary young men have had the honour to be seen by the gentlemen of the faculty, Royal Society, and other admirers of natural curiosity, who allowed them to surpass anything of the same kind ever offered to the public. Their address is singular and pleasing, their persons truly shaped and proportionate to their height, and affords an agreeable surprise: they excel the famous Maximilian Miller, born in 1674, shewn in London in 1733; and the late Swedish giant will scarce admit of a comparison. To enumerate every particular, would be too tedious; let it suffice to say, that they are beyond what is set forth in ancient or modern history. The ingenious and judicious who have honoured them with their company have bestowed on them the most lavish encomiums, and on their departure have express’d their approbation and satisfaction. In short the sight of them is more than the mind can conceive, the tongue express, or pencil delineate, and stands without a parallel in this or any other country.”*

### Charles Hamilton 1795–1829

Born in 1795, Charles Hamilton, was a native of County Down and measured 7 feet 6 inches (2.29 m) in height. He was mentioned in the newspapers as “certainly the tallest man in the kingdom”. He died in London on 26 August 1829 after a 6-month illness. According to the *Morning Journal* he left “*a wife and five children, the youngest only 12 months, in Ireland, totally unprovided for*” and had “*not left funds to defray the funeral expenses*”.

### Patrick Murphy 1834–1862

Patrick Murphy was born on a farm in Killowen near Rostrevor, County Down on 15 June 1834 [48]. His parents, his sister and brother were all of ordinary size. By 5 years of age he wore shoes more convenient for 9-year-old children and at the age of 13, he was already 6 feet (1.83 m) tall. As a young man Patrick Murphy worked as labourer at Liverpool docks and later as a waiter at a hotel where he started to draw large crowds. He subsequently began a career as showman in Liverpool and later in Europe. In 1857, the Emperor and Empress of Austria, Franz Joseph I and Elisabeth (“Sisi”) invited him

to appear before them [3]. Several unofficial sources claimed an adult height of between 8 feet 1 inches (2.46 m) and 8 feet 10 inches (2.69 m). However, in about 1864 he was measured by the German physician, anthropologist and pathologist Rudolf L.K. Virchow (1821–1902) in Berlin and was found to be 7 feet 3.4 inches (2.22 m) tall [49].

In 1860, at the age of 28 he died of smallpox at Marseille, France [3, 23]. His embalmed body was brought back to Ireland, and he was buried in Kilbroney cemetery on 18 June 1862. There is a long-standing but unsubstantiated claim that a stone-filled coffin was buried in Kilbroney and that the skeleton of Patrick Murphy was kept in a museum in Marseille [50].

### Francis Sheridan 1841–1870

Francis (“Big Frank”) Sheridan was born in County Cavan to Patrick Sheridan and Catherine Prior. He had one brother and four sisters. His family moved to Hawick in the Scottish Borders during the Famine. Sheridan was 7 feet 8 inches (2.34 m) in height and weighed 22 stone (140 kg). He was landlord of the Irish Harp Tavern, Baker Street, Hawick, Scotland. He died in 1870 and is buried in Wellogate Cemetery in Hawick.

The text on the gravestone reads:

*“ERECTED BY PATRICK SHERIDAN IN MEMORY OF HIS SON FRANCIS SHERIDAN WHO DIED AT HAWICK 12TH AUGUST 1870 AGED 29 YEARS. He was 7 feet 8 inches in height.”*

### James Allender 1848–1886

James Allender was a Derry-born gardener reportedly measured 7 feet 6 inches in height (2.29 m). He travelled to Baltimore, Maryland in 1876 to enter showbusiness and stated that he had a taller brother. He died in July 1886 aged 38, in the workhouse in South Shields, England after a 7-week illness and is buried at Westoe cemetery, England. According to the New Zealand newspaper *Hawke’s Bay Herald* of the 13 August 1886: *“This gives another proof of the fact that these overgrown samples of humanity seldom live long; being in spite of their massive appearance, weak as to the action of the heart, and feeble also as regards other vital functions”*.

### George Parsons - Pat O’Brien 1853–1888

George Parsons was born in Belfast in 1853 and succeeded (James) Hugh Murphy Jr as “Barnum’s Irish Giant” after Murphy’s death [35]. His stage name was Patrick William O’Brien (Pat O’Brien). Although often advertised with a height of 7 feet 3.5 inches (2.22 m) and even up to 8 feet 4 inches (2.54 m), his real height was probably no more than 6 feet 11 inches (2.11 m). On 20 November 1883 he married the 6 feet 7.5

inches (2.02 m) tall German, Christiana Dorothea Dunz in Pittsburgh, Pennsylvania and she adopted a new showbusiness name, Annie O’Brien (Fig. 5a). The couple worked for the Great Barnum Show for two seasons and met U.S. president Grover Cleveland. On 21 April 1885, Annie O’Brien gave birth to a boy Brian O’Brien. The child reputedly weighed 20 pounds at birth and was nearly 2 feet (61 cm) in length (Fig. 5a). In late 1886 the couple decided to tour England, Scotland, Ireland and Germany. George Parsons died on 21 March 1888 in London, England after several months of illness.

### Simon McCann 1855–1900

Simon McCann was born in 1855 in Knockbride, County Cavan. He was a member of a known Irish *AIP* p.(R304\*) kindred which included two relatives with gigantism. His height was 7 feet 4 inches (2.24 m) and given his descendants’ history he is assumed to be heterozygous for the same *AIP* variant [6]. He died in 1900.

### Hugh Murphy 1870-?

Captain Hugh Murphy was born in Carnlough, County Antrim in 1870. His parents were of short stature both measuring less than 5 feet (1.52 m). He first worked as Queen’s Life Guard, but in 1897 he went to the United States to become Barnum and Bailey’s third “Irish Giant”. He was billed at 7 feet 6 inches (2.29 m) and 8 feet 2 inches (2.49 m) tall. His real height, according to photographic evidence, was around 7 feet 2 inches (2.18 m). The date, place and cause of his death are unknown (Fig. 5b).

### Bernard McCrystal 1884–1905

Bernard McCrystal was born in 1884 in Omagh, County Tyrone, which is in the geographical *AIP* p.(R304\*) hotspot and reached a height of 7 feet (2.13 m). He died in 1905.

### James McCooke c. 1890–1967

James McCooke was identified during the mid-Ulster *AIP* screening study. In 1901, he lived in Garvagh, Derry, where he was a student. He was married to Stephanie Maud McCooke and fathered seven children. He was pictured at the height of 7 feet (2.13 m) after arrival in Western Australia in 1910 [6]. He died on May 1, 1967, at the age of 77 in the Beverly district of Western Australia.

### John Johnston 1898–1918

John Johnston was born in 1898 in Maghera, Derry. He was pictured in 1918 in the *Daily Sketch* where his height was



**Fig. 5** (a) George Parsons (1853–1888) alias Patrick William O'Brien (Pat O'Brien), billed as "Barnum's Irish Giant" and Christiana Dorothea Dunz (1863–1902) alias Annie O'Brien and their baby boy, Brian (1885?). Cabinet card from 1886 in the collection of W. W. de Herder. (b) Captain Hugh Murphy (1870–), "The Irish Giant" and wife. Cabinet card in the collection of W. W. de Herder. (c) Newspaper photograph from the Daily Sketch (May 1918) of John Johnston (2.11 m) from Maghera, Derry on arrival in Canada. He was a relative of an *AIP* p.(R304\*) screening carrier from the mid-Ulster region [6]

said to be 6 feet 11 inches (2.11 m; Fig. 5c). Some weeks after his arrival in Regina, Saskatchewan, he reportedly spoke of tiredness and headaches and he died shortly afterwards from a hypertensive crisis; he is presumed to have been an *AIP* p.(R304\*) heterozygote [6].

## The discovery of the Ulster *AIP* founder variant

The *AIP* p.(R304\*) founder variant came to light due to a combination of historical research, medical genetics, patient experiences and local knowledge. Together these elements uncovered heretofore unsuspected links between patients not only in the North of Ireland but also internationally. It is a remarkable example of how modern genetics can provide insights into historical disease profiles, and conversely how this information can inform improved patient management in the future. A key initial clue came in 2008 from the attendance of a 20-year-old male pituitary adenoma patient from the North of Ireland at the Department of Endocrinology at St. Bartholomew's Hospital (Bart's) in London. When exploring the family history, the patient told of a first cousin with pituitary gigantism. As this represented a new FIPA kindred, the germline sequence of *AIP* was tested—at

the time still as a research test—and identified a p.(R304\*) pathogenic variant in both cousins [14].

Memories of conversations many years before with Prof. Michael Besser, the previous head of the Endocrinology Department at Bart's and himself a leading figure in pituitary disease management, then became highly relevant. He had encouraged his trainees to visit the Hunterian Museum just a few miles down the road from Bart's to view the skeleton of Charles Byrne, the 'Irish Giant'. The hypothesis now arose whether there could be a link between the 'Irish giant' and this new FIPA kindred. As a reference centre for neuroendocrinology research and treatment, Bart's had developed a sizeable population of patients with pituitary adenomas. Exploring the historical patient cohort at Bart's led to the identification of 3 other patients hailing from the island of Ireland. Among these was the other key individual in the research discovery, Brendan Holland, who had been diagnosed and treated for pituitary gigantism by Prof. Besser since the early 1970s [14]. Mr. Holland (6 feet 10 inches (2.09 m)) combined his own personal insights into the lived experience of developing a pituitary gigantism with his deep local knowledge about his birthplace of County Tyrone. Genealogical enquiries quickly revealed multiple FIPA kindreds with gigantism, acromegaly and prolactinoma [14]. These included Brendan Holland's family, as recounted in

print and documentaries [16, 51–53]. The historical aspect came into greater focus as attention turned to the skeleton of Charles Byrne. By then the research group had noted the familial links between Byrne and his cousins the Knipe twins described above, which led them to suspect that also represented a proto-FIPA kindred. Remarkably, the birthplaces of multiple individuals from the North of Ireland—including Byrne and his cousins—mapped to a relatively small region to the west of Lough Neagh in Ulster. Further genetic analyses demonstrated that all the affected individuals shared the *AIP* p.(R304\*) variant and also had a common haplotype at microsatellite markers surrounding *AIP*, demonstrating that the propensity for pituitary adenomas and gigantism was inherited from a common source. Following extraction of DNA in a specialist laboratory in Germany—to avoid contamination at the London laboratory dealing with high quality DNA from patients with the same suspected gene variant—genetic studies using DNA extracted from Byrne's teeth revealed both the *AIP* p.(R304\*) variant and the common haplotype with the contemporary Irish cases. This established the link from historical to modern day gigantism in the North of Ireland *via* a common genetic risk. The *AIP* p.(R304\*) variant cohort was expanded to multiple other individuals and families with pituitary adenomas that originated from mid-Ulster, thereby definitively confirming an *AIP* genetic hotspot in 2011 [14]. Derived from this research, the concept of a common *AIP* p.(R304\*) ancestral founder arose, which was, with the help of further families in 2017, estimated to date to about 2500 years ago. That date range encompasses possible ancient gigantism cases that might have inspired myths of Irish giants [6, 14].

Over the following decade research projects across Ireland and the UK mapped the extent of the genetic hotspot further, identifying numerous unaffected carriers and leading to early diagnosis of pituitary adenomas in some pre-symptomatic individuals [6, 54]. Following this discovery, a population screening study was undertaken in the geographic *AIP* hotspot around the North of Ireland. A total of almost 1,000 participants were screened and six individuals in mid-Ulster were discovered to be heterozygous for *AIP* p.(R304\*) [6]. There are two further pathogenic/likely pathogenic *AIP* variants (c.3G>A; p.(M1I) and c.442\_444del; p.(L148del)) discovered on the island of Ireland, but as yet only *AIP* p.(R304\*) has been associated with a diagnosis of gigantism [6, 55].

To date, 29 *AIP* p.(R304\*) kindreds thought to have originated from the North of Ireland founder variant have been diagnosed. This now includes contemporary heterozygotes in Scotland, England, USA and Australia. Work continues on the extensive cascade genetic testing required for these kindreds.

## Contemporary individuals with gigantism from Ireland

### Brendan Holland 1952 – Present

Brendan Holland is a man living with gigantism who was born in Dungannon, County Tyrone close to the birthplaces of a number of historical Irish giants (Fig. 6) [14]. As noted above, he is heterozygous for the p.(R304\*) *AIP* variant and has dedicated decades to furthering research into gigantism, particularly on the island of Ireland. He is a co-author on the study which highlighted the increased prevalence of this condition in Ireland [6]. Brendan, his story and the experiences of relatives with gigantism due to the p.(R403\*) *AIP* variant have also been central to various documentaries and news articles relating to giants in Ireland [16, 51–53]. More recently he has co-written a book with a fellow patient who is also heterozygous for the Irish *AIP* p.(R304\*) variant living in the US (see below) [16]. This book details their and other relatives' experiences of living with pituitary adenomas and gigantism from the 1970s onwards.



**Fig. 6** Map of Ireland indicating the places of birth of historical individuals with a reliable history of gigantism. Numbers refer to the listing of individuals discussed in the text. The approximate birth region of a present-day individual with gigantism due to the *AIP* p.(R304\*) founder variant is indicated with an asterisk

## Niamh Feeney 1981 – Present

Niamh Feeney from County Sligo is a niece of Brendan Holland who also detailed her lived experiences in documentaries and the book *In Search of Giants* [16, 51]. She experienced rapid growth due to a GH-secreting pituitary adenoma from around the age of 13, reaching a height of 6 feet 3.5 inches (1.92 m). Her experience highlights the significant challenges that patients living with gigantism continue to face in the current day.

## Individuals with gigantism in the Irish diaspora

Numerous individuals with gigantism that were born in North America, Australia, and the UK have been reported to possess direct Irish ancestry.

One such person living with tall stature and with confirmed Irish ancestry is Colleen Snyder [16]. She is heterozygous for *AIP* p.(R304\*), has a height of 1.83 m and developed a GH-secreting pituitary adenoma as a child. Along with Brendan Holland she describes her experience of living with a pituitary adenoma and has shared photographic evidence of her onset of rapid growth at around 4 years of age. Following her own research and after contacting Brendan Holland and Professor Márta Korbonits it became evident that her family originated from the same Ulster geographic hotspot where others that are heterozygous for the Irish *AIP* p.(R304\*) continue to live and be diagnosed [16, 51–53]. Her maternal great uncle suffered from acromegaly, based on photographs.

Bernard A. Coyne (8 feet 4 inches (2.54 m)) was born in 1897 in Oto, Woodbury County, Iowa to Catherine “Kate” O’Connell Coyne (1.57 m) and Sylvester Coyne (1.73 m). Bernard’s paternal grandmother, Rose Anne Carr Coyne (1827–1915), was born in County Cavan, and died in Iowa.

James D. (Jim) Porter (1811–1859), who was 7 feet 8 inches (2.335 m) tall, was born in Portsmouth, Ohio and died in Louisville, Kentucky, USA. Porter was widely known as “Big Jim Porter – The Kentucky Giant”. During his travels in the United States, Charles Dickens described meeting him in 1842 in his book “*American Notes for General Circulation*” [56]. Porter’s mother, Sarah Harrington (1785–1872), was born in Ireland.

Henry Marion Mullins (1915–1978) was 7 feet 6.75 inches (2.31 m) tall and was known by his stage name as “Henry Hite”. Mullins was born in Atlanta, Georgia, and he reported that he had Irish ancestors.

Robert Buchannan Keenan (1893–1935) who reached a height of 7 feet 2 inches (2.18 m), was born in Carnegie, Allegheny County, Pennsylvania; he was also noted to have Irish ancestry.

May Walsh was born on 5 July 1887 in Chicago, Illinois, to James Walsh (born 1849) and Bridget (Ryan) Walsh (born

1850), both of Spruce Hill, Roscrea, County Tipperary. At the age of 33, May stood 6 feet 5¾ inches (1.98 m) tall when she was admitted to the Municipal Tuberculosis Sanatorium in Chicago in 1921, where she died of pulmonary tuberculosis on 18 July 1922.

Dennis Francis Duffy was born in Rutherglen, Victoria, Australia on 21 April 1907 to Patrick Duffy and Margaret Francis, who were from County Armagh. He had a twin brother named John. While he claimed be the world’s tallest man at 8 feet 5.5 inches (2.58 m), his true height was more likely closer to 7 feet 6 inches (2.29 m). He played the role of an Irish Guardsman Dennis Duffy/Dinny Duffy/Dennis O’Duffy to increase interest among audiences. He joined Wirths Circus in Rutherglen at the age of 17 and later joined John Lester’s Revue in England. In 1935, he was the focus of attention at a medical convention in Bournemouth, UK. He decided to will his body after his death with the proviso that 1000 pounds were to be paid to his next of kin. In 1939, he married Alma James, a Canadian colleague at the Revue (3 feet tall (91 cm)). Dennis Duffy later returned to Australia where he continued touring until a year before his death at the age of 50 on 26 June 1957.

John Frances Carroll was the subject of a medical case report in 1961 by Prezio et al. [57]. Born in Buffalo, New York in 1932, John F. Carroll (also known as the “Buffalo Giant” in medical literature) is the third-tallest individual in history. Due to his red hair, John F. Carroll was also known as “Big Red”, and “Red Carroll.” He was afflicted with both acromegalic gigantism and severe kyphoscoliosis. He was the son of John J. Carroll (1899–1966, Buffalo, Erie County, New York, USA) and Johanna “Hannah” Evans Carroll (1901–1979, Tralee, County Kerry, Ireland). His birth weight was 9 pounds and 5 ounces (4.2 kg), and he grew up as a healthy child. He had a healthy sister who was of normal height. Carroll was said to have had numerous relatives with tall stature (some in excess of 7 feet in height) on both sides of his family, but no definitive supporting evidence of this was identified. He was the tallest child in his elementary school class, standing 5 feet 6 inches (1.68 m) at the age of 12. While on the Bishop Timon High School basketball team he was 6 feet 2 inches tall (1.88 m) when he was 16 years old, and he was incredibly strong compared to his teammates. Carroll’s rapid height gain continued into the age of 20 when he stood 7 feet (2.13 m) tall. By age 22, he was 7 feet 6 inches (2.29 m) tall. During that period, he developed kyphoscoliosis and decreased muscle strength and a leg deformity meant that he had to resort to crutches. Of note he reported never having completed puberty and had scant body and facial hair; a testicular biopsy demonstrated atrophy and abnormal Leydig cells. His maximum standing height was 8 feet (2.44 m). He had numerous falls and leg fractures, and by his mid-twenties he had developed cardiomegaly and other marked signs of acromegaly. Radiologically, his sella turcica was markedly enlarged indicating a pituitary macroadenoma

and he eventually received external radiotherapy. He died in New York in August 1969 at the age of 37 due to renal failure.

## Uncertain cases

### James MacDonald?–1760

The Annual Register for 1760 reported that James MacDonald, who attained a height of 7 feet 6 inches (2.29 m), died at his home near Cork at the great age of 117 years on 20 August 1760. MacDonald abandoned his career as a touring performer because it confined him too much and he allegedly chose the more “active life” in the army. After his return to Ireland in 1716, he worked as a day-labourer until a few years before his death. It seems likely in this instance that not only was MacDonald’s height exaggerated, but also his age. Edward J. Wood notes: “*for giants live rarely to be old men and still rarer to be centenarians; while dwarfs on the contrary, often attain a venerable age*”. This historical statement is scientifically correct and evidence-based [3].

### Shawn Nabontree c1786-1856

On December 6, 1856, the Mayo Constitution published the obituary of a giant named Shawn Nabontree: “*One of the last of the mythical line of Irish giants, in the person of Shawn Nabontree, died at Connemara, Ireland, on Friday last. He owed his sobriquet to his unusual stature, being a man of extraordinary athletic symmetry-namely, seven feet (2.13 m) in height, and weighing over twenty stone (280 pounds). His family, the Joyces, has been for many years one of the wonders of Connemara. He died at the age of seventy, and has left four stalwart sons*” [3].

Unfortunately, this report was almost entirely erroneous or invented. The deceased individual was a Mr. Seán (John) Joyce, who lived in a region bordering Connemara in the west of Ireland. He was not remarkably tall (1.80 m., 5 feet 11 inches) with fair hair and was known as Seán Bán (Fair Seán) to distinguish him from other similarly named Joyce family members. In retelling, the name “Seán Bán” possibly became the root of *Shawn-Nabon*.

### Thomas Reid, “The Monaghan infant giant”

Thomas Reid, was a baby documented in letters to have been born in Glaslough, Monaghan on the 17th of December 1859 and baptised the next day in the parish of Donagh to parents Patrick and Anne Reid. His growth was reportedly normal until the age of 6 months, before reaching a weight of 5 stone (31.8 kg) and height > 3 feet (91.4 cm) at 18 months. Around this age, his parents exhibited him in the

Rotundo (Rotunda), Dublin but little is known about what happened to him following this. From a modern medicine perspective, his reported clinical phenotype could be consistent with X-linked acroigantism [58, 59].

### Big Magee

A giant nicknamed “Big Magee” from Clogher, County Tyrone was described on in an autobiographical account of the author William Carleton (1794–1869) in 1896 and in a poem by Benjamin Lyness in 1842 [60].

### Donadea giant

In 1790 it was reported that a coffin measuring 10 feet 4 inches (3.15 m) in length, was unearthed from a depth of seventeen feet in a peat bog at Donadea, County Kildare containing a skeleton 8 feet 2½ inches (2.50 m) tall, with a 7 feet (2.13 m) spear [3, 61].

### Mullingar giant

A skeleton measuring more than 7 feet (2.13 m) in length with a large skull, a large jaw and large hand bones in line with its size, was found in a grave among other human remains in 1861 in Mullingar, County Westmeath, when workmen were digging next to the parish church [3].

### Cruit Island Giant

The Cruit Island Giant was a 7 feet 8 inches (2.34 m) tall adolescent skeleton said to have been unearthed in 1954 in Cruit Island in Donegal by road workers when digging into a sand and gravel bank while affecting road repairs. A local doctor and a dentist were brought to the scene. Due to the dark, they had to examine the giant bones on the beach using a car’s headlights. The physicians noted that the skeleton’s wisdom teeth had not yet emerged, suggesting that the individual was a late adolescent. They also remarked on the even wear and complete lack of decay on the teeth, which pointed to a coarse, ancient diet before death. The bones were gathered and reinterred in an unmarked plot in the nearby Cill Bhríde cemetery. Unsuccessful attempts to exhume the remains were chronicled in a documentary by the BBC in 2018 [53]. The remains are said to be interred elsewhere in the cemetery.

### “O’Briens” & “Murphys”

Due to the fame of notable Irish individuals with gigantism in the 17th and 18th centuries, the names O’Brien and Murphy subsequently became popular artistic names and served to hint

at Irish roots. George Auger/William Henry Auger was 2.26 m (7 feet 5 inches) tall and lived from 1881 to 1922. He was born in Cardiff, Wales and died in Manhattan, New York, USA. During his on-stage appearances in France his artistic name was “Patrick O’Brien”. A 1.97 m (6 feet 5.5 inches) tall individual “Elsbeth Murphy” was born around 1842–1843 and originated from Vienna, Austria. She toured mainland Europe the 1860s [62]. A 2.19 m (7 feet 2 inches) tall woman named “Maggie Murphy” appeared at Steeplechase Park, Coney Island, New York, USA in 1897. She may be the same individual as Marie/Maria Schubiger/Schubinger who was born in in Sankt Gallen in Switzerland and who supposedly toured with another tall person, claiming to be brother and sister.

## Discussion

In this review we have used historical manuscripts, adverts, press articles, media and medical literature to compile the most complete account to date of gigantism among Irish-born individuals and those with strong evidence of Irish roots. Historical descriptions of many of the cases suggest that these individuals had pituitary gigantism. In the pre-scientific era these people experienced the unopposed effects of pituitary tumour growth and excess hormonal secretion, leading to extreme tall stature, and cardiovascular and musculoskeletal morbidity. Consequently, many died young and in ill health. These historical records are in line with what we know today regarding the clinical profile of pituitary gigantism [9]. Despite the availability of modern diagnostics and treatment strategies, pituitary gigantism is still a very challenging condition that affects paediatric and adolescent patients. Distinguishing abnormal from normal growth at presentation and referring individuals for diagnostic imaging and hormonal testing can lead to significant delays in instituting effective surgical or medical treatment. In pituitary gigantism delayed diagnosis is important, as control of height before or during the pubertal growth spurt is vital to limit the severity of excessive adult stature [9, 11].

A major feature that distinguishes pituitary gigantism from typical, adult-onset acromegaly is the role of genetics. About 50% of subjects with pituitary gigantism have a constitutive or mosaic germline causative factor, as compared to only a few percent of adult acromegaly populations [9, 11]. The most frequent of these are germline pathogenic variants in *AIP* (about 30%), X-linked acrogigantism (10%) and McCune-Albright syndrome (5%) [11, 12].

The role of genetics in pituitary gigantism in Ireland is now well established, with a pathogenic p.(R304\*) *AIP* variant having been identified in the skeleton of Charles Byrne and in multiple contemporary patients throughout Ulster and beyond [6, 14–16]. Many individuals in the North of Ireland

or originating from this area who presented with gigantism, acromegaly, or prolactinoma share the *AIP* p.(R304\*) variant and the associated haplotype, indicating that they represent a single, large kindred [6, 14, 15]. The p.(R304\*) *AIP* variant represents a hotspot (due to the presence of a CpG island); it is the most frequent pathogenic *AIP* variant described with numerous independent occurrences across the globe, including other founder effects [13, 54, 63, 64].

The impact of this *AIP* founder would have remained limited to that small region of Ulster were it not for a long history of population flux spreading Irish genetic heritage to nearby counties and later globally. Since the establishment of the *AIP* founder up to 2500 years ago, major demographic, cultural and political changes took place across the region [6, 14]. This period spans the emergence of Irish Celtic culture, the dawn of the Christian era, the rise of feudal Gaelic kingdoms and the Plantation of Ulster. Regional population links between Ulster and other areas like Scotland are extensive, including the kingdom of Dalriada in 5th century, the influx of Scottish tenants during the Plantations in the 17th century, and emigration from Ireland to urban centres like Glasgow in the 19th century and beyond. Work is ongoing to establish whether contemporary patients living with gigantism in Scotland are related to those in the North of Ireland. Establishing such a link would establish a scientifically reasonable origin for myths of Irish and Scottish giants discussed above.

Emigration further afield to the United States, initially by Presbyterian Scots Irish in the 18th century and the later massive wave from throughout Ireland (including Ulster) during and after the Great Famine in the 1840s acted to spread Irish ancestry globally. Recent evidence has identified a direct link between the Irish *AIP* founder to at least one Irish American family [16]. Individuals with gigantism from *AIP* p.(R304\*) kindreds also emigrated to Canada and Australia and it is plausible that later subjects with gigantism in regions of high Irish emigration shared this genetic aetiology [16]. Genetic testing in pituitary adenoma populations internationally has benefitted from increased awareness of the *AIP* p.(R304\*) variant in those with family roots in the North of Ireland [52]. This highlights the clinical value of international collaborations on rare, disease-causing genetic variants (Fig. 5.)

Our compilation identifies multiple individuals with pituitary gigantism with links to Ireland and traditional Irish emigrant centres. To accumulate more than 25 publicly known cases of such a rare condition relating to a relatively small Irish population is remarkable. Other living and deceased individuals with gigantism from Ireland are not individually detailed here for reasons of confidentiality. In addition, there is the high probability of other historical gigantism cases going undocumented. Many individuals have clear links to the North of Ireland where the p.(R304\*) *AIP* variant is highly prevalent (Table 1). Regarding the

**Table 1.** Historical individuals with gigantism from Ireland listed in chronological order of their reported dates of birth

| Name                      | Born                                         | Died          | Age | Height (ft in/m)          | Place of Birth<br>Town, County        |
|---------------------------|----------------------------------------------|---------------|-----|---------------------------|---------------------------------------|
| Edmond Malone             | 1665                                         | ?             | ?   | 7'7"/2.31 m               | Portlester,<br>Meath                  |
| Mary Murphy               | 1673                                         | After<br>1701 | ?   | 7'2.13 m                  | Portrush,<br>Antrim                   |
| James Kirkland            | ca. 1730                                     | ?             | ?   | 7'1"/2.17 m               | Ballygar,<br>Galway                   |
| Cornelius Magrath         | 1736                                         | 1760          | 24  | 7'5"-8"/<br>2.26-2.34 m   | Silvermines,<br>Tipperary             |
| Thomas Fanton             | 1745                                         | 1782?         | 37  | 8'0"-8'3"/<br>2.44-2.51 m | Omagh,<br>Tyrone                      |
| Patrick Cotter            | 1760                                         | 1806          | 46  | 8'1"/2.46 m               | Kinsale, Cork                         |
| Charles Byrne             | 1761                                         | 1783          | 22  | 7'7"/2.31 m               | Littlebridge,<br>Drummulan,<br>Tyrone |
| Knipe Twins               | c.1761                                       |               |     | 7'2"/2.18 m.              | Magherafelt,<br>Derry                 |
| Charles Hamilton          | 1795                                         | 1829          | 34  | 7'6"/2.29 m.              | Down                                  |
| James Clancy              | 1812                                         | ?             | ?   | 7'2"/2.18 m.              | Arklow,<br>Wicklow                    |
| Eliza Simpson             | c.1828                                       | ?             | ?   | 7'-7'2"/<br>2.13-2.18 m.  | Bantry, Cork                          |
| Patrick Murphy            | 1834                                         | 1862          | 28  | 7'3.4"/2.22 m.            | Killowen,<br>Down                     |
| James Patrick<br>Tolley   | c.1839                                       | ?             | ?   | 7'5"/2.26 m.              | Carlow                                |
| Francis Sheridan          | 1841                                         | 1870          | 29  | 7'8"/2.34m.               | County Cavan                          |
| (James) Hugh<br>Murphy Jr | 1842                                         | 1875          | 33  | 7'1.5"/2.17 m.            | Waterford,<br>Waterford               |
| James Allender            | 1848                                         | 1886          | 38  | 7'6"/2.29 m.              | Derry, Derry                          |
| George Parsons            | 1853                                         | 1888          | 35  | 6'11"/2.11 m.             | Belfast,<br>Antrim                    |
| Simon McCann              | 1855                                         | 1900          |     | 7'4"/2.24m                | Tipperary                             |
| Hugh Murphy               | 1870                                         | ?             | ?   | 7'2"/2.18 m.              | Carnlough,<br>Antrim                  |
| Thomas Dalroy             | late 19 <sup>th</sup> -early<br>20th century | ?             | ?   | 7'6.5"/2.30 m.            | Kildare                               |
| Patrick O'Connor          | 1881                                         | 1922          | 41  | 7'4"/2.23 m.              | Tipperary                             |
| Bernard McCrystal         | 1884                                         | 1905          | 29  | 7'0"/2.13m                | Omagh,<br>Tyrone                      |
| John Johnston             | 1898                                         | 1918          | 20  | 6'11"/2.11m               | Maghera,<br>Derry                     |
| James McCooke             | circa 1890                                   | 1967          | ?   | 7'0"/2.13m                | Garvagh,<br>Derry                     |
| Michael Grealish          | 1892                                         | ?             | ?   | 7'9"/2.36m                | Bohola, Mayo                          |
| Jim Cully                 | 1922                                         | 1981          | 59  | 7'2"/2.18 m.              | Tipperary                             |

Individuals from Ulster or with suspected links to p.(R304\*) kindreds are shaded in grey

remaining cases, the aetiology of their pituitary gigantism remains speculative. Some might have unknown links to the North of Ireland, others might have been due to other *AIP* variants. Pituitary gigantism has multiple genetic causes apart from *AIP*, and about 50% of cases are still without a known genetic cause, so it is likely that in Ireland like elsewhere, a variety of genetic culprits can be suspected in individuals with pituitary gigantism [9].

Lough Neagh, the largest freshwater lake in Ireland, was fabled to have been created by the giant Fionn MacCumhaill when he scooped up earth to throw at his nemesis, the Scottish giant Benandoner. Kindreds heterozygous for the *AIP* p.(R304\*) founder variant continue to be diagnosed in a genetic hotspot around Lough Neagh at a rate of approximately one new family every 1–2 years (unpublished data and [6]). Results described in this review and ongoing research in pituitary adenoma populations show that Irish giants were not entirely mythical but occurred as part of a scientific reality that remains highly relevant to medicine today.

## Declaration

**Conflict of Interest** The authors declare that they have no conflict of interest.

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