

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte YUQIAO SHEN, TERRY HERMISTON, and ALI FATTAEY

Appeal 2008-0827
Application 10/191,922
Technology Center 1600

Decided: October 30, 2008

Before TONI R. SCHEINER, LORA M. GREEN, and
RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 1, 2, 5, 6 and 8-10.¹ We have jurisdiction under 35 U.S.C. § 6(b).

¹ Claims 3 and 4 are also pending, and are objected to as being dependent on a rejected base claim (App. Br. 5).

STATEMENT OF THE CASE

The claims are directed to a type 5 adenovirus mutant. Claim 1 is representative of the claims on appeal, and reads as follows:

1. An isolated type 5 adenovirus mutant, comprising at least one mutation in the i-leader nucleotide sequence of the viral major late transcriptional unit of the type 5 adenovirus, wherein said at least one mutation causes truncation of an i-leader protein encoded by said i-leader nucleotide sequence.

We affirm.

ISSUE (Enablement)

The Examiner concludes the Specification enables an adenovirus type 5 of SEQ ID NO: 1, mutated to comprise a C→T mutation of nucleotide 8350, but does not reasonably provide enablement for any mutation in the i-leader sequence of any adenovirus type 5 which causes any truncation of the i-leader protein.

Appellants contend that the Specification teaches the skilled artisan how to make and use the full scope of the claimed invention.

Thus, the issue on Appeal is: Whether the skilled artisan could practice the full scope of the claimed invention?

FINDINGS OF FACT

FF1 According to the Specification, “[c]onditionally replicating viruses represents a promising new class of anti-cancer agents,” noting that “[d]erivatives of human adenovirus type 5 (Ad5) have been developed that selectively replicate in, and kill, cancer cells.” (Spec. 1.)

FF2 The Specification teaches further:

Two general genetic approaches have been taken for developing oncolytic viruses with enhanced anti-cancer properties. The first is targeted genetic manipulation, in which certain viral genes, or regulatory elements (i.e. promoters) are deleted, or foreign genes inserted, etc. Although this approach has been successfully utilized to construct many novel viruses, its application is limited by the requirement of a thorough understanding of the biology of that virus. Even in the case of Ad5, one of the most extensively studied viruses, such information is not always available or complete. Thus, targeted genetic manipulations are in many cases very difficult to make. The second approach is genetic selection under carefully controlled conditions. Viruses selected in this fashion grow preferentially under that particular condition. In essence, this is a natural evolution process, only occurring under carefully controlled conditions in the laboratory.

(Spec. 1-2 (references omitted).)

FF3 Thus, the Specification teaches that an “object of the invention is to describe genetically altered adenoviruses, preferably Ad 5, with favorable anti-cancer activity produced using random mutagenesis and subsequent bio-selection on cancer cells wherein the mutagenesis causes at least one mutation in the i-leader sequence of the viral major late transcriptional unit.”

(*Id.* at 2.)

FF4 In the methods taught by the Specification, Ad5 was treated with nitrous acid to induce random mutagenesis (*id.* at 9). The mutagenized virus was repeatedly passaged on human cancer cell lines, and then assayed for cytolytic activity (*id.*)

FF5 Two Ad5 mutants were isolated, ONYX-201 and ONYX-203, with ONYX-201 being about 500- to 1000-times more active than Ad5, and ONYX-203 being 30- to 50- times more active than Ad5 (*id.* at 13).

FF6 The genomes of ONYX-201 and -203 were sequenced, and each contain seven single point mutations (*id.* at 15). The Specification teaches that each had a C to T mutation at nucleotide 8350 that is “necessary and sufficient for the increased cytolytic activity of ONYX-203. . . .[and] also necessary to account for the superior cytolytic activity of ONYX-201.” (*Id.* at 16.)

FF7 According to the Specification:

Intending not to be bound by any particular theory to account for the anti-cancer activity of the invention viruses, we note that the C to T mutation at nucleotide 8350 completely accounts for the cytolytic activity of ONYX-203, and is required for the activity of ONYX-201. This mutation is located in the i-leader of the major late transcription unit of Ad5. The i-leader sequence is spliced to a subset of L1 mRNA, which predominantly encodes the 52/55K protein, and may modulate expression of the 52/55K protein. The i-leader itself contains an open reading frame that codes for a 145-amino acid protein, i-leader protein. The exact roles of the 52/55K protein and the i-leader protein in adenovirus replication are not clear. They are the only proteins encoded in the major late transcription unit that are expressed prior to viral DNA replication. This suggests that these two proteins may have an important role in the initiation of viral DNA replication. The C to T mutation at nucleotide 8350 changes the codon for Gln at amino acid 125 to a stop codon UAG, thus eliminating the last 21 amino acids of the i-leader protein. It is thus thought that this changes the expression of the i-leader protein and the 52/55K protein, and thus affects viral replication to produce favorable anti-cancer activity.

(*Id.* at 16-17 (references omitted).)

FF8 The Specification also teaches the use of the mutagenized Ad5 in the treatment of cancer (*id.* at 17-20).

FF9 Claims 1, 2, 5, 6, and 8-10 stand rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the Specification does not enable the full scope of the invention (Ans. 7).

FF10 According to the Examiner, “the specification, while being enabling for an adenovirus type 5 of SEQ ID NO: 1, mutated to comprise a C→T mutation of nucleotide 8350, does not reasonably provide enablement for any mutation in the i-leader sequence of any adenovirus type 5 which causes any truncation of the i-leader protein.” (*Id.*)

FF11 The Examiner made the following findings with respect to the factors set out in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).²

FF12 *Nature of the Invention*: The Examiner notes that the “invention is in the nature of mutated adenovirus i-leader sequences which cause truncations to the i-leader protein such that increased cytolytic activity in cancer cells is produced.” (Ans. 7.)

FF13 *Breadth of Claims*: According to the Examiner, the claims are drawn to any truncation of the i-leader protein, wherein such truncations “encompass C-terminal and N-terminal deletions, internal deletions, as well as missense mutations which confer these deletions.” (Ans. 7.) The Examiner notes further that the Specification teaches that the mutation of the adenovirus type 5 mutants is “to provide for adenoviruses having cytolytic

² The factual considerations discussed in *Wands* are: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

activity of cancer cells,” arguing that “these mutants must be enabled for providing increased cytolytic activity for the breadth of the mutations claimed.” (*Id.*)

FF14 *State of the Prior Art*: The Examiner relies on Soloway³ and McCormick⁴ to demonstrate the state of the prior art (Ans. 8). According to the Examiner, Soloway teaches mutations in the i-leader sequence of a type-5 adenovirus, and that when such mutations remove the potential for synthesis of the i-leader protein, the major late protein synthesis during the adenovirus infection cycle is stabilized (*id.*). The Examiner finds that Soloway does not provide any discussion of increased cytolytic activity of the Ad5 virus in cancer cells (*id.*). McCormick is cited for teaching several mutations in the E1A and E1b regions that confer increased cytolytic activity in p53 and pRb cancer cells, but does not discuss the i-leader sequence (*id.*). The Examiner thus asserts that “from the Art alone, the Artisan would fail to be able to reasonably predict that a truncation of the i-leader sequence could provide favorable anticancer activity, much less which portions may be truncated to produce such activity.” (*Id.*)

FF15 *The Direction and Guidance provided by Appellant*: The Examiner first notes that the Specification broadly discloses “the use of lytic viruses, particularly adenoviruses, for the selective lysis of cancer cells, and strategies of making and using such viruses.” (Ans. 9) The Specification, the Examiner notes, discusses two specific mutants, ONYX 201 and 203, but

³ Soloway, “The Adenovirus Type 5 i-Leader Open Reading Frame Functions in *cis* To Reduce the Half-Life of L1 mRNAs,” *J. Virol.*, Vol. 64, No. 2, pp. 551-558 (1990).

⁴ McCormick, US Patent No. 5,677,178, issued October 14, 1997.

does not provide guidance as to “which regions of the i-leader sequence can be truncated to produce favorable anticancer activity.” (*Id.*) The Examiner finds that “outside of the broad concepts outlined by Appellant, there is little in the way of specific guidance or specific direction for the making of the adenovirus which have deletions in the i-leader protein and provide the required activity,” that is, “the Artisan would have to make the adenovirus truncated mutant, and test it to find out if it provided the activity, for the vast majority of embodiments encompassed.” (*Id.* at 9-10.)

FF16 *The Existence of Working Examples*: According to the Examiner, while “Applicants have shown *in vitro* transfection and selective increased lysis of cancer cells with adenoviral vectors comprising a mutation, from C to T, at nucleotide position 8350 of specific adenovirus type 5, Applicants have not shown which other regions(s) of the i-leader protein may be deleted to confer this increased anticancer activity.” (Ans. 10.)

FF17 *The level of Skill in the Art and Lack of Predictability*: The Examiner acknowledges that the level of skill is high, being an M.D. or a Ph.D., but asserts that “it is not reasonably predictable which truncations would provide for increased anticancer activity, beyond the single truncation repeatedly found and demonstrated in the specification.” (Ans. 10-11.)

FF18 *Undue Experimentation*: The Examiner finds that it would require an undue amount of experimentation to practice the claimed invention (Ans. 11). Specifically, the Examiner concludes that because “the experimentation required to reasonably predict the working embodiments beyond the single mutation disclosed as necessary and sufficient to confer the anticancer

activity, encompasses the vast majority of embodiments claimed, such breadth is considered not enabled as it is undue.” (*Id.* at 11.)

PRINCIPLES OF LAW

“When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application.” *In re Wright*, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993).

“[T]o be enabling, the specification . . . must teach those skilled in the art how to make and use *the full scope of the claimed invention* without ‘undue experimentation.’” *Wright*, 999 F.2d at 1561, (emphasis added), *quoted in Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, (Fed. Cir. 1997). Thus, “there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed.” *In re Vaeck*, 947 F.2d 488, 496 & n. 23, (Fed. Cir. 1991), *quoted in Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1374, (Fed. Cir. 1999).

ANALYSIS

Appellants argue that they have taught how to make the claimed invention, as the Specification describes making genetically altered Ad5, as well as their subsequent bioselection on cancer cells and identification of mutants having the desired anti-cancer activity (App. Br. 18-19).

Appellants argue further that the Specification teaches how to use the claimed invention (*id.* at 20). Specifically, Appellants argue that they “have taught that the adenoviral mutants of the present invention replicate significantly better than the parental virus in cancer cells” and “demonstrate significantly higher cytolytic activity toward tumor cells relative to normal cells.” (*Id.*) Thus, Appellants assert that they “have taught how to make and use the entire scope of the claimed invention without undue experimentation.” (*Id.*)

We agree. The Examiner has not established that the amount of experimentation to practice the full scope of the claimed invention would not have been routine. The Examiner’s rejection is essentially premised on the fact that the Specification only discloses a single Ad5 mutation that results in a truncation in the i-leader protein and demonstrates cytolytic activity.

The Specification, however, teaches how to make Ad5 mutants, as well as methods of screening for mutants that have the desired activity (FF4), and thus the guidance and Examples provided in the Specification demonstrate that the skilled artisan would be able to determine other Ad5 mutants having a truncation in the i-leader sequence that have cytolytic activity without undue experimentation. Therefore, the Examiner has not established that it would require an undue amount of experimentation to produce Ad5 mutants that are truncated in the i-leader sequence, or that it would require an undue amount of experimentation to determine which of those mutants would have cytolytic activity. *See, e.g., Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1360 (Fed. Cir. 1998) (“test [for undue experimentation] is not merely quantitative ... if it is merely routine).

Stated differently, the Examiner states that it would not have been predictable which truncations would provide increased anticancer activity (Ans. 10-11). It is the Examiner's burden to establish lack of enablement. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). In this case, the Examiner did not provide sufficient evidence nor provide adequate scientific reasoning to support this conclusion in view of Appellants' success in isolating mutations that result in truncation of the i-leader protein.

CONCLUSIONS OF LAW

Thus, we conclude that the Examiner has not established that the skilled artisan could not practice the full scope of the claimed invention, and the rejection is reversed.

ISSUE (Written Description-New Matter)

The Examiner finds that the Specification does not provide a generic description or teaching of type-5 adenovirus mutants that have a truncation in the i-leader sequence and also have cytolytic activity against cancer cells.

Appellants contend - relying heavily on the ONYX-201 and ONYX-203 mutants, which have C to T mutation at nucleotide 8350 changes the codon for Gln at amino acid 25 to a stop codon UAG, thus eliminating the last 21 amino acids of the i-leader sequence - that the disclosure as filed provides support for an Ad5 mutant that contains at least one mutation in the i-leader sequence of the viral major late transcriptional unit, wherein said at least one mutation causes truncation of an i-leader protein.

Thus the issue on Appeal is: Whether the disclosure of the ONYX-201 and ONYX-203 mutants that have the C to T mutation at nucleotide 8350 which changes the codon for Gln at amino acid 25 to a stop codon UAG, thus eliminating the last 21 amino acids of the i-leader sequence, is sufficient written description for the generic recitations of type-5 adenovirus mutants that have a truncation in the i-leader sequence as recited in claim 1?

FINDINGS OF FACT

FF19 We reference FF1-FF8 made above with respect to the enablement rejection.

FF20 The Specification discloses that an object of the invention is to “describe genetically altered adenoviruses, preferably Ad 5, with favorable anti-cancer activity produced using random mutagenesis and subsequent bio-selection on cancer cells wherein the mutagenesis causes at least one mutation in the i-leader sequence of the viral major late transcriptional unit.” (FF3.) We find, however, that the Specification and claims as originally filed do not generally disclose an isolated type 5 adenovirus mutant, comprising at least one mutation in the i-leader sequence of the viral major late transcriptional unit of the type 5 adenovirus, wherein said at least one mutation causes truncation of an i-leader protein.

FF21 Rather, the Specification only talks about the truncation of the i-leader sequence in the context of ONYX-201 and ONYX-203.

FF22 The Examiner rejects claims 1, 2, 5, 6, and 8-10 under 35 U.S.C. § 112, first paragraph “as failing to comply with the written description requirement, as comprising new matter.” (Ans. 4.) According to the

Examiner, the claims contain “subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (*id.*).

FF23 The Examiner initially notes that the “claims subject to this rejection comprise adenovirus type 5 viruses with a generic truncation of the coding sequence encoding the i-leader protein.” (Ans. 4.)

FF24 The Examiner finds that the Specification discloses that mutations in the i-leader sequence may lead to increased cytolytic activity in cancer cells (Ans. 5). The Examiner finds further that the Specification provides “an experimental screen to randomly mutate adenoviruses to find those with the increased cytolytic activity,” and also finds adenoviruses with such activity, determining that a C to T mutation, which truncates the last 21 amino acids of the i-leader protein, conferred increased cytolytic activity (*id.*).

FF25 The Examiner finds, however, that the Specification does not provide a generic description or teaching of type-5 adenovirus mutants that have a truncation in the i-leader sequence (Ans. 5).

FF26 The Examiner finds further:

given that Appellant and the Artisan, did not even understand the function of the i-leader protein (e.g., SPECIFICATION, p. 16, paragraph 3), the Artisan would not have understood Appellant to have been in possession of a generic truncation if the i-leader sequence, which includes generic deletions of the i-leader protein, which comprises both longer and shorter C-terminal deletions, N-terminal deletions, and internal deletions, and of any generic size, as well as frameshift (missense) mutations which cause deletion of the amino acids, with substitution by another set of amino acids of the same or distinct sizes.

(Ans. 5-6.)

FF27 The Examiner concludes that “the blaze marks to demonstrate possession of the invention appear to be absent, and instead, the claimed invention appears to rely on obviousness, which is not sufficient to demonstrate possession.” (Ans. 6.)

PRINCIPLES OF LAW

The requirement for written description under the first paragraph of section 112 is separate and distinct from the enablement requirement of that paragraph. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, (Fed. Cir. 1991). “Although there is often significant overlap” between the enablement and written description requirements, “they are nonetheless independent of each other.” *University of Rochester*, 358 F.3d at 921. An “invention may be enabled even though it has not been described.” *Id.* *See also Ex parte Kubin*, 83 USPQ2d 1410, 1416-17 (Bd. Pat. App. & Int. 2007).

In the context of new matter, the disclosure as originally filed need not provide “*in haec verba* support for the claimed subject matter at issue,” rather, the disclosure should convey to one skilled in the art that the inventor was had possession of the invention at the time of filing. *Purdue Pharma L.P. v. Faulding Pharmaceutical Co.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000) (citations omitted). The *Purdue Pharma* court cautioned that “the disclosure must . . . convey with reasonable clarity to those skilled in the art that . . . [the inventor] was in possession of the invention,” that is “one skilled in the

art, reading the original disclosure, must immediately discern the limitation at issue in the claims.” *Id.* (alterations in original).

Furthermore, although not explicitly drawn to the issue of new matter, with respect to claims drawn to biological matter, such as the adenovirus mutants claimed here, we find *University of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997), and its progeny to be instructive, as when an original claim is not supported by written description support, a claim added by amendment would also likewise not be supported.

“A written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as by structure, formula, [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” *Lilly* at 1568. The claims in *Lilly* were directed generically to vertebrate or mammalian insulin cDNAs. *See id.* at 1567. The court held that a structural description of a rat cDNA was not an adequate description of these broader classes of cDNAs.

The *Lilly* court explained that

a generic statement such as . . . ‘mammalian insulin cDNA,’ without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Id. at 1568. Finally, the *Lilly* court set out exemplary ways in which a genus of cDNAs could be described:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Id. at 1569.

Our appellate reviewing court revisited the issue of describing DNA. *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956 (Fed. Cir. 2002). The *Enzo* court held that a claimed DNA could be described without, necessarily, disclosing its structure. The court adopted the standard that “the written description requirement can be met by ‘show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics . . . i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.’” *See id.* at 964 (emphasis omitted, ellipsis and bracketed material in original).

Our appellate review court has also noted that “*Eli Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.” *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003).

ANALYSIS

Appellants argue that support for claim 1 can be found throughout the disclosure as filed (App. Br. 10). Appellants assert that the Specification clearly teaches “that appellants considered the invention to embrace an adenovirus comprising at least one mutation in the i-leader sequence of the viral major late transcriptional unit.” (*Id.* at 11.)

Appellants rely specifically on Table 1,⁵ which presents a summary of mutations in ONYX-201 and ONYX 203, the relevant part of which is reproduced below (Amendment of January 9, 2006, p. 39).

Table 1. Summary of mutations in ONYX-201 and ONYX-203.

Site	Mutation	Presence	Gene affected
8350	C to T	201 and 203	i leader -- Truncate the i-leader protein; may change viral gene expression and replication

Appellants argue that the table includes “reference to mutations that ‘Truncate i-leader protein.’” (App. Br. 11.) That, along with the discussion in the specification that the “C to T mutation at nucleotide 8350 changes the codon for Gln at amino acid 25 to a **stop codon UAG, thus eliminating the last 21 amino acids of the i-leader protein**” (App. Br. 11 (quoting Spec. 16-17)) demonstrate that “appellants identified truncation mutations of the i-leader sequence as capable of providing oncolytic viruses that have favorable anti-cancer activity.” (App. Br. 11.)

Appellants’ arguments are not convincing. The only mutation that results in the truncation of the i-leader protein disclosed by the disclosure as

⁵ Table 1 as added to the Specification in an amendment dated January 9, 2006 (Evidence Appendix A).

originally filed is the C to T mutation at site 8350 (FF21). The disclosure as originally filed, however, never discusses mutations that result in truncation of the i-leader protein outside of the C to T mutation at site 8350 (FF21).

The Specification further discusses targeted genetic manipulations in the development of oncolytic viruses, teaching that “its application is limited by the requirement of a thorough understanding of the biology of that virus. Even in the case of Ad5, one of the most extensively studied viruses, such information is not always available or complete. Thus, targeted genetic manipulations are in many cases very difficult to make.” (FF2.) And the Specification does not disclose such a thorough understanding of the function of the i-leader sequence. In fact, the Specification acknowledges that the “exact roles of the 52/55K protein and the i-leader protein in adenovirus replication are not clear.” (FF7.) Moreover, in speaking of the biology of the truncation of the i-leader protein, the Specification only discusses it in the context of the C to T mutation at position 8350, teaching that the “C to T mutation at nucleotide 8350 changes the codon for Gln at amino acid 125 to a stop codon UAG, thus eliminating the last 21 amino acids of the i-leader protein. It is thus thought that this changes the expression of the i-leader protein and the 52/55K protein, and thus affects viral replication to produce favorable anti-cancer activity.” (FF7.)

Thus, while the disclosure generically supports methods of mutating the Ad5 virus and then testing for cytolytic activity, and also supports the specific mutation of C to T at position 8350 that results in truncation of the i-leader protein as well as increased cytolytic activity; the disclosure as originally filed does demonstrate that the skilled artisan would understand

that the inventors considered Ad5 mutants that generically have a mutation that results in truncation of the i-leader sequence resulting in increased cytolytic activity as part of the invention. As discussed above, it is admitted in the Specification that the role of the i-leader is “not clear” (FF7). Thus, the teaching that truncation at amino acid 125 produced increased cytolytic activity would not immediately be recognized as a general property of other mutants truncated at different positions in the i-leader sequence. In other words, the skilled artisan, reading the original disclosure, would not immediately discern the limitation of an Ad5 mutant “comprising at least one mutation in the i-leader sequence . . . [that] causes a truncation of an i-leader protein encoded by said i-leader nucleotide sequence.” (Claim 1.)

Second, even if claim 1 had been an originally filed claim, we find that it would not have been supported by adequate written description. Claim 1 is drawn to “[a]n isolated type 5 adenovirus mutant, comprising at least one mutation in the i-leader sequence of the viral major late transcriptional unit of the type 5 adenovirus, wherein said at least one mutation causes truncation of an i-leader protein encoded by said i-leader nucleotide sequence.” The only use disclosed for such viruses taught by the Specification is that they have cytolytic activity, and thus are useful in therapeutic methods for the treatment of cancer (FF3, FF8; *see also* App. Br. 20 (“**[A]ppellants have taught . . . how to use the claimed invention. . . . [teaching] that the adenoviral mutants of the present invention replicate significantly better than the parental virus in cancer cells . . . and**

demonstrate significantly higher cytolytic activity toward tumor cells relative to normal cells.”.)

We acknowledge that the scope of claim 1 is not expressly limited to Ad5 mutants that have a mutation that cause truncation of an i-leader protein that have cytolytic activity against tumor cells; claim 1, however, does encompass Ad5 mutants that display such increased cytolytic activity against tumor cells, and in fact, that is the only use disclosed in the Specification for the claimed Ad5 mutants. Appellants, however, have not disclosed any other position in the i-leader sequence at which truncation results in the desired cytolytic activity except for the C to T mutation at nucleotide 8350.

Thus, while Appellants have described how to make and test Ad5 mutants that fall within the scope of claim 1, such that the enablement requirement is satisfied, they have not described which positions within the i-leader sequence would lead to truncation mutants that would have cytolytic activity such that the skilled artisan could visualize and/or recognize the remaining members of the genus. Thus, under *Lilly* and its progeny, the Specification does not show possession of a sufficient number of Ad5 mutants within their genus to establish possession of their claimed genus. *Cf. Enzo*, 323 F.3d at 964 (“if the functional characteristic of ... binding to [CD48] were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed,” the written description requirement may be met). Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, (“definition by function ... does not suffice

to define the genus because it is only an indication of what the gene does, rather than what it is”); *see also Kubin*, 83 USPQ2d at 1416-17.

CONCLUSION

We thus affirm the rejection of claim 1 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, we find that the disclosure of the ONYX-201 and ONYX-203 mutants that have C to T mutation at nucleotide 8350 changes the codon for Gln at amino acid 25 to a stop codon UAG, thus eliminating the last 21 amino acids of the i-leader sequence, is not sufficient written description for the generic recitations of type-5 adenovirus mutants that have a truncation in the i-leader sequence as recited in claim 1.

Claims 2, 5, 6, and 8-10, fall with claim 1 as Appellants did not argue those claims separately, and the rejection is affirmed as to those claims as well. *See* 37 C.F.R. § 41.37(c)(1)(vii). 1.192(c)(7)

Appeal 2008-0827
Application 10/191,922

TIME LIMITS

No time period for taking any subsequent in connection with this appeal may be extended under 37 C.F.R. § 1.136 (a).

AFFIRMED

Ssc:

ONYX PHARMACEUTICALS, INC.
2100 POWELL STREET
12TH FLOOR
EMERYVILLE, CA 94608