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Official Ref.:	EP 15 195 765.1 / EP 3 034 627
Patentee:	The Trustees of Columbia University in the City of New York
Opponent:	ILLUMINA INC.
Our Ref.:	I09472EPOP/DB

In the name and on behalf of

Illumina, Inc.
5200 Illumina Way
San Diego, CA 92122 USA

we herewith file an opposition against the European Patent EP 3 034 627 B1 entitled "MASSIVE PARALLEL METHOD FOR DECODING DNA AND RNA", which was granted to "The Trustees of Columbia University in the City of New York". The mention of the grant of the patent was published on 30 January 2019.

We authorize the deduction of the opposition fee from our deposit account no. 28 000 741.

A. Requests

1 It is herewith requested that the patent EP 3 034 627 B1 (in the following also referred to as "the opposed patent" or "EP'627") be revoked in its entirety on the basis of

- Article 100 (a) EPC (the subject matter of the opposed patent is not patentable under Articles 56 EPC);
- Article 100 (b) EPC (the opposed patent does not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art according to Article 83 EPC); and
- Article 100 (c) EPC (the subject-matter of the opposed patent extends beyond the content of the application as filed contravening Article 123(2) EPC and beyond the content of the earlier application as filed contravening Article 76(1) EPC.

2 Should the Opposition Division not be in a position to grant the above request to revoke the opposed patent in its entirety, oral proceedings are requested as an auxiliary measure.

B. Cited documents

3 The following prior art documents are cited in the context of the opposition grounds:

D1: Alberts et al., "Molecular Biology of the Cell", Third Edition, Garland Publishing Inc., New York (1994), pp. 98-103

D2: US 5,608,063 (Hobbs I), published on March 4, 1997

D3: US 5,151,507 (Hobbs II), published on September 29, 1992

D4: WO 91/06678 A1 ("Tsien")

D5: M. B. Welch et al., Chem. Eur. J. 1999, 5(3), pp. 951-960

D6: B. B. Rosenblum et al., Nucleic Acids Research 1997, 25(22), pp. 4500-4504

D7: J. M. Prober et al., Science 1987, 238(4825), pp. 336-341

D8: B. Canard et al., PNAS 1995, 92, pp. 10859-10863

D9: R. Gigg et al., Journal of the Chemical Society 1968, 1903-1911

D10: N. Ramzaeva et al., Helvetica Chimica Acta 1995, 1083-1090

D11: Seela et al., Bioorganic & Mechanical Chemistry Letters 1995, 5:3049-3052

D12: N. Ramzaeva et al., Helvetica Chimica Acta 1997, 80:1809-1822

D13: US 5,547,839 („Dower")

D14: M. L. Metzker et al., Nucleic Acids Research 1994, 22(20), pp. 4259-4267

D15: WO 00/53805 A1 ("Stemple")

4 The opposed patent EP 3 034 627 B1 has a filing date of 5 October 2001 and claims priority of two US applications filed on 6 October 2000 and 26 June 2001. Documents D1 to D15 were published before the priority date of the opposed patent, and therefore constitute state of the art under Article 54(2) EPC.

5 Further, reference is made to the following evidence submitted during the examination proceedings of the opposed patent by the Proprietor.

D16: Declaration of the inventor Jingyue Ju, Ph. D. as filed on 12th March 2018

6 We also refer to the decision by the Examining Division rejecting the parent application EP 1 790 736 A2:

D17: Decision of the Opposition Division dated 23 March 2015 regarding EP 1 790 736 A2.

7 **D18** provides an overview of decisions by the USPTO PTAB revoking US counterparts to EP'627.

C. The opposed patent

8 The opposed patent pertains to a specific aspect of DNA sequencing by synthesis (see below).

9 In the following, we will set forth some principles underlying DNA sequencing in general and particularly DNA sequencing by synthesis as they were known before the priority date.

10 It is respectfully submitted that this will help appreciate the subsequent arguments that the claims as granted are not disclosed by the application as filed, that the subject matter of the claims cannot be worked across the scope of the claims by the person skilled in the art without an undue burden and that the claimed subject matter is obvious over the prior art.

I. Background

1. Structure of DNA

11 DNA consists of two complementary strands that wind around one another to form a double helix.[1] The strands of DNA are made up of individual deoxyribonucleotides (also referred to as "nucleotides"), which are composed of deoxyribose (i.e. a sugar with five carbon atoms, that lacks the 2'-OH group that ribose normally contains), a nucleobase (also referred to as "nitrogenous base"), and a phosphate group. There are four different nucleotides in DNA, which differ from each other by their nitrogenous bases: adenine (A), cytosine (C), guanine (G), and thymine (T). The nucleotides in each strand are linked by their phosphate groups, which in each case attach the 5' carbon atom of the deoxyribose of one nucleotide to the 3' carbon atom of the deoxyribose of the next nucleotide, to form the sugar-phosphate backbone of the DNA strand as shown in Figure 1 below.

12 The two complementary strands assemble together by base-pairing with the formation of hydrogen bonds between the bases, where C pairs with G and A pairs with T, as also shown in Figure 1 below. The C-G and A-T pairs are also commonly referred to as Watson-Crick base pairs.

[1] See D1, pp. 98-102.

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