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Cartas científicas

QnrVC, a new transferable Qnr-like family

QnrVC, una nueva familia Qnr transferible

Dear Sir,

QnrVC, was described in 2008, within an integron environment in *Vibrio cholerae*.[1] Further studies have described QnrVC-like sequences, either in *V. cholerae* or other microorganisms, located within integrons or plasmids, some of them able to be transferred within microorganisms.[2–7]

This work analyses the phylogenetic relationships of QnrVC respecting the 5 established plasmid-encoded Qnr-families, searching GenBank for QnrVC-related sequences.[8]

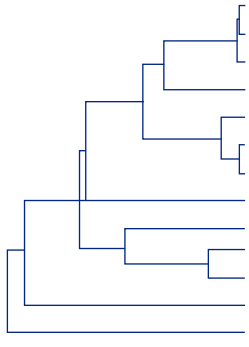
A GenBank search was performed using the nucleotide (GenBank: EU436855) and amino acid (GenBank: ACC54440.2) sequences of QnrVC1/VC3 as template, selecting those sequences with identities levels higher than 70% with respect to QnrVC1/VC3.[8]

Those selected sequences and representative sequences of the established Qnr-families present in http://www.lahey.org/qnrStudies, were included in the phylogenetic studies.

The BIOEDIT software was used to perform an *in silico* alignment to establish the presence of the characteristic loops A and B structures.[9]

Ten different Qnr sequences, which following established criteria[8] may be classified within a common family together QnrVC1/VC3, were found in GenBank (Fig. 1). Thus, 6 chromosomal-encoded sequences (ADI81040 and EGQ95960 from *V. cholerae*; YP132629 and EAS42881 from *Photobacterium profundum*; EGU51872 or EEX92304 from *Vibrio orientalis*; YP_002263022 from *Allivibrio salmonicida*: 3 plasmid-encoded (1 from *Aeromonas caviae* – ADI55014; 1 from *Vibrio fluvialis* – found under 3 different GenBank entries: AEM62764, AER42862 or AER42863; and QnrC) and an ORF from *Acinetobacter baumannii* (DNA GenBank: GU944730), without information about its chromosomal or plasmid encoding, were detected. This ORF, found within a class 1 integron, shows the transferability of QnrVC-like from water-borne microorganisms towards a relevant nosocomial pathogen.[6] Besides, sequences with internal stop codons were also found, as QnrVC2 (GenBank: AB200915) present in the pVN84 of *V. cholerae*.[1]

The plasmid-encoded QnrVC-like (QnrVC4) present in *A. caviae* have also been recently introduced in GenBank as detected in river-isolated microorganisms such as *Escherichia coli* (JQ837999.1), *A. hydrophyla* (i.e.: JQ838001.1), in both encoded within a class 1 integron, *Pseudomonas* sp. (i.e.: JQ838008.1), or other *Aeromonas* spp. (JQ838004.1). QnrC shows identities >70% with the remaining potential QnrVC sequences, except EAS42881 (*P. profundum*) and YP_002263022 (*A. salmonicida*) (Fig. 1). This phylogenetic nearby between QnrC and members of the QnrVC family, previously noted by Wang et al.,[10] suggests the *Vibrionaceae* genus as the ancestral chromosomal source of QnrC.



GenBank access[1]	Qnr nomenclature[2]	Microorganism	Location		Identity matrix												
					1	2	3	4	5	6	7	**8**	9	10	11	12	13
EGQ95960		*V. cholerae*	Chromosome	1		99	99	82	79	80	81	**72**	71	75	75	63	66
ADI55014	QnrVC4	*A. caviae*	Plasmid	2			99	82	80	81	81	**72**	72	76	76	64	65
AEM62764		*V. fluvialis*	Plasmid	3				83	80	81	82	**72**	72	76	76	64	66
EGU51872		*V. orientalis*	Chromosome	4					78	80	80	**72**	72	73	72	59	65
ADI81040	QnrVC3	*V. cholerae*	Chromosome	5						98	98	**72**	69	72	71	63	61
ORF[3]		*A. baumannii*	N.I.	6							99	**73**	70	72	71	65	62
ACC54440	QnrVC1/VC3[4]	*V. cholerae*	Chromosome	7								**74**	70	72	72	65	62
ACK75961	**QnrC**	***P. mirabilis***	**Plasmid**	**8**									**67**	**70**	**68**	**60**	**64**
YP_002263022		*A. salmonicida*	Chromosome	9										78	77	65	65
YP132629		*P. profundum*	Chromosome	10											97	62	66
EAS42881		*P. profundum*	Chromosome	11												62	66
BAD88776	QnrS1		Plasmid	12													60
AAL60061	QnrA1		Plasmid	13													

Fig. 1. Phylogenetic relationships among *qnrVC*-like genes. The distance-based tree was generated by using p distance with the neighbour-joining method. 1: only one GenBank access is indicated for each different Qnr sequence included in the figure, as indicated in the text, QnrVC4 has also been described in other microorganisms. 2: specific nomenclature present in the literature. When the sequence has been published or introduced in Genbank as an erroneous member of an established Qnr family has not been considered. 3: located within the GenBank DNA sequence No. GU944730. 4: introduced in GenBank as QnrVC1 in 2008,[1] but a posterior correction in the sequence results in a sequence 100% identical to GenBank sequences ADI81036 and ADI81043 introduced as QnrVC3.[3] In the absence of an established nomenclature we refer to this sequence as QnrVC1/VC3. 5: YP_002263022 (*A. salmonicida*) has been claimed as a representative of a novel Qnr-family, however it is not plasmid encoded and many other QnrVC-like were previously described, then we considered that will be more correct considered as a potential member of the QnrVC family. N.I.: non-information about its genetic location is disposable. In the identity matrix, QnrC has been noted in bold, and identities of QnrC with remaining sequences have been highlighted.

A serious confusion statement was observed among GenBank entries. Thus, 5 entries, in which a QnrVC-like was found, were recorded as QnrB1, other 2 as QnrC (both different that currently described QnrC), and two different sequences as QnrVC3. Similarly, the ORF present in sequence GU944730, it is not reported in GenBank as encoding a QnrVC-like gene, but it has been introduced in INTEGRALL (http://integrall.bio.ua.pt/), an internet repository devoted to integrons, as encoding a QnrVC1b protein, and recently published as QnrVC-like.[6]

Finally, the Qnr loops A and B, essential for the activity of different Qnr proteins,[9] were predicted in all QnrVC-related proteins. Thus, QnrVC-like may be considered as full functional Qnr-like proteins.

In conclusion, a series of sequences that may be including within a new common transferable Qnr-family have been found in GenBank. The close similarity (higher than 70%) between the QnrC and QnrVC families may suggest the need for nomenclature unification following the current established normative.

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Anemia hemolítica en un niño con malaria tratado con arthemeter

Hemolytic anemia in a child with malaria treated with arthemeter

Sr. Editor:

La malaria o paludismo es una enfermedad parasitaria que en el año 2010 ocasionó la muerte a 665.000 personas a escala mundial, de las que el 86% eran niños menores de 5 años[1]. Los casos de malaria importada son cada vez más frecuentes en nuestro país debido al incremento de la inmigración y los viajes internacionales. La OMS recomienda actualmente la terapia combinada con artemisina (TCA) como fármacos de primera línea para el tratamiento de la malaria por *Plasmodium falciparum* no complicada y grave, tanto en niños como en adultos[2-4]. Estos fármacos producen un rápido aclaramiento de la parasitemia y una pronta mejoría de los síntomas[5]. Son por lo general muy bien tolerados, presentando muy escasos efectos adversos[2]. En varios países de Europa se han comercializado recientemente.

Presentamos el caso de un niño natural de Mali que recibió tratamiento para la malaria en su país de origen con arthemeter intramuscular (i.m.) y que ingresa por persistencia de la malaria y anemia hemolítica. Se trata de un varón de 7 años que acude a urgencias por malestar general y fiebre de 24 h de evolución. Nacido en Mali, residía en España desde los 3 años de edad hasta que se trasladó hace un año de nuevo a Mali con su padre. Ambos regresaron a España una semana antes del ingreso. El padre informa que estuvo ingresado en un hospital de su país 2 semanas antes con diagnóstico de malaria, siendo tratado con un fármaco por vía i.m. durante 3 días. La exploración inicial mostró una temperatura de 37,8 °C, ictericia conjuntival y hepatomegalia.

En la analítica al ingreso destacaba leucocitosis con neutrofilia (308.000 plaquetas/mm^3) y datos de anemia hemolítica (Hb 6,9 g/dl, bilirrubina total 2,98 mg/dl (B. directa: 0,63 mg/dl), LDH 1,274 UI/l (110-295), y 8% de reticulocitos. El test de Coombs directo fue negativo, así como el resto de estudios de autoinmunidad. No se constató déficit de G6PDH. Se realizaron frotis sanguíneos al ingreso y a las 8 h, que fueron negativos. El test de diagnóstico rápido para malaria (inmunocromatografía) y la PCR de malaria fueron positivos para *P. falciparum*. Estos hallazgos se atribuyeron al episodio de malaria padecido en Mali 3 semanas antes. El resto de estudios serológicos (incluyendo VIH) y parasitológicos fueron negativos.

El paciente recibió una transfusión de un concentrado de hematíes, con mejoría clínica y analítica progresiva. Sucesivos frotis durante su ingreso fueron negativos. Mediante fax se obtiene el tratamiento recibido para la malaria en Mali: arthemeter intramuscular: primer día 80 mg (4,2 mg/kg) y segundo y tercer días 40 mg (2,1 mg/kg).

A las 2 semanas del alta hospitalaria, en frotis sanguíneo de control se objetiva la presencia de hematíes parasitados (1/1.000) con formas en anillo de *P. falciparum*. En este momento el paciente no presentaba datos de hemólisis activa y mantenía muy buen estado general. Se inició tratamiento oral con sulfato de quinina (10 mg/kg/8 h) 5 días y clindamicina (40 mg/kg/8 h) durante 7 días. El test de resistencia a fármacos antimaláricos se informó como presencia de resistencia exclusivamente a cloroquina. Tras el tratamiento, el paciente quedó totalmente asintomático, con normalización de todos los parámetros sanguíneos.