27th ECCMID Vienna, Austria 22 – 25 April 2017
The congress of ESCMID

Session: P086 Skin and soft-tissue infections

Category: 2e. Skin, soft tissue, bone & joint & central nervous system infections

25 April 2017, 12:30 - 13:30
P1792

Panton-valentine leucocidin positive CC121 strain methicillin-sensitive Staphylococcus aureus is associated with pyomyositis in Cambodian children

Bernadette Young[1], Sona Soeng[2], Poda Sar[2], Varun Kumar[3], Vuthy Sar[3], Songly Hor[3], Rachel Bousfield[4], Kate Emary[5], Emma Nickerson[4], Nicole Stoesser[6], Christopher Parry[7], Npj Day[5], Daniel Wilson[8], Catrin Moore*[9]

[1]*University of Oxford; Nuffield Department of Medicine*

[2]*Cambodia-Oxford Medical Research Unit*

[3]*Angkor Hospital for Children*

[4]*Addenbrooke's Hospital*

[5]*University of Oxford*

[6]*University of Oxford; Nuffield Department of Clinical Medicine*

[7]*Liverpool*

[8]*Nuffield Department of Medicine, Experimental Medicine Division, University of Oxford, John Radcliffe Hospital, Wellcome Trust Centre for Human Genetics, University of Oxford*

[9]*University of Oxford; Centre for Tropical Medicine and Global Health*

Background: Pyomyositis is primarily a disease of children in tropical regions. 90% of cases are caused by *Staphylococcus aureus*. Only small case series have been reported, and the bacterial genetic factors underlying this disease are incompletely understood. We present a genome wide association study of *S. aureus* isolated from pyomyositis and asymptomatic carriage from the same human paediatric population.

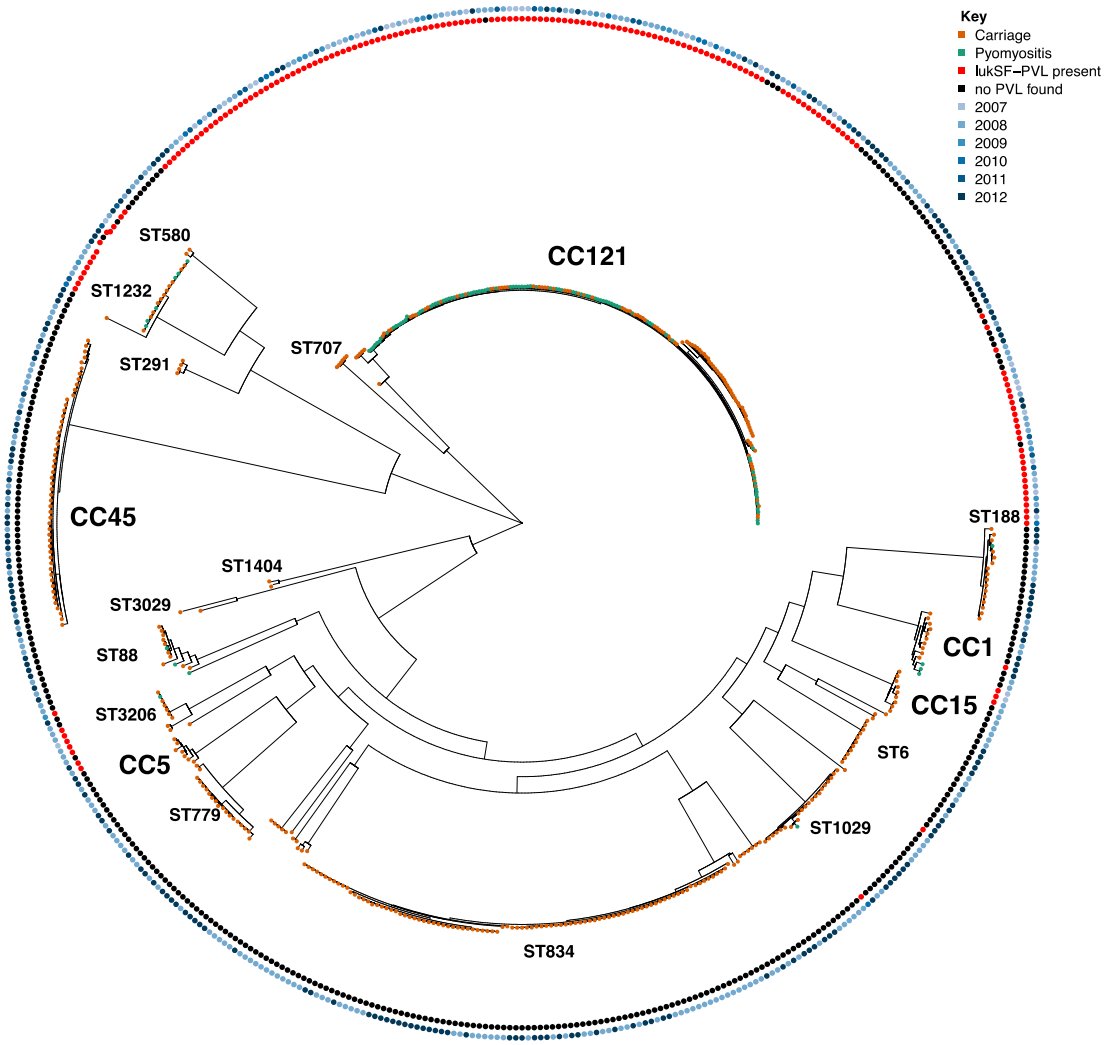
Material/methods: Bacterial isolates were identified from 102 children, attending Angkor Hospital for Children in Siem Reap, Cambodia over a six-year period 2007-12, who had a clinical diagnosis of pyomyositis and *S. aureus* cultured from the abscess samples. 418 *S. aureus* nasal carriers were identified from two studies of *S. aureus* carriage in the same population in 2008 (n=222) and 2012 (n=196).

A single isolate was cultured from each clinical sample and underwent whole-genome sequencing on the Illumina HiSeq platform, yielding 520 high quality sequences. Single nucleotide polymorphisms (SNPs) were identified after mapping reads against a reference genome (MRSA252) and *de novo* assembly was performed using Velvet. We tested for loci associated with pyomyositis by performing association testing for all SNPs and short sequences (kmers) using Gemma, which controls for bacterial population structure. We examined strains associated with pyomyositis using Bugwas, which identifies bacterial lineages and tests them for association with phenotype. Multi-locus sequence type was determined *in silico* using blast.

Results: The phylogeny of *S. aureus* isolated from asymptomatic carriage and pyomyositis shows that 87/102 (85%) of pyomyositis isolates are found within a single clade (Figure) (p=1.6x10^{-30}). These isolates belong to Clonal Complex (CC) 121. In contrast, carriage isolates include a global diversity of global lineages, including CC121, as well as CC1, CC5, CC15, CC45. Strikingly, 41 carriage isolates form a sub-clade within CC121 and no cases of pyomyositis are observed in this sub-clade. This lineage is strongly associated with carriage rather than pyomyositis (p=4x10^{-14}). Both CC121 lineages were found as asymptomatic carriers in 2008 and 2012.

In addition to lineage effects, we find a strong association between the presence of Panton-Valentine leucocidin (PVL) and pyomyositis, even after controlling for population structure (p=5x10^{-20}). Kmers mapping to PVL were found in 99/102 (97%) of pyomyositis isolates, compared with 84/418 (20%) of carriage isolates. PVL is a known *S. aureus* virulence factor, and is often carried by CC121, but is absent from the protective carriage sub-clade. PVL was not limited to CC121 isolates in this study, but is found in multiple lineages (Figure).

Conclusions: We have discovered strong evidence for bacterial genetic determinants for this relatively neglected, serious bacterial disease using a non-selective method with no prior assumptions. We find both lineage and gene specific effects, with an overwhelming association between PVL and pyomyositis in Cambodian children.


Key
Carriage
Pyomyositis
lukSF−PVL present
no PVL found
2007
2008
2009
2010
2011
2012
ST580
ST1232
ST291
CC121
ST707
CC45
ST188
ST1404
ST3029
ST88
CC1
CC15
ST3206
CC5
ST6
ST779
ST1029
ST834