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A presentation of the differences between the sheep and goat genetic maps

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Abstract – The current autosomal version (4.2) of the sheep genetic map comprises 1175 loci and spans ~3540 cM. This corresponds to almost complete coverage of the sheep genome. Each chromosome is represented by a single linkage group, with the largest gap between adjacent loci being 19.8 cM. In contrast the 1998 goat genetic map (the most recently published) is much less well developed spanning 2737 cM and comprising only 307 loci. Only one of the goat chromosomes appears to have complete coverage (chromosome 27), and 16 of the chromosomes are comprised of two or more linkage groups, or a linkage group and one or more unlinked markers. The two maps share 218 loci, and the maps have been aligned using the shared loci as reference points. Overall there is good agreement between the maps in terms of homologous loci mapping to equivalent chromosomes in the two species, with only four markers mapping to non-equivalent chromosomes. However, there are lots of inversions in locus order between the sheep and goat chromosomes. Whilst some of these differences in locus order may be genuine, the majority are likely to be a consequence of the paucity of genetic information for the goat map.

genetic / linkage / sheep / goat / map

1. INTRODUCTION

Fossil evidence suggests that the sheep and goat lineages diverged approximately five to eight million years ago, and that the Caprinae lineage itself diverged from that of Bovinae 17 to 20 million years ago. Despite this difference in divergence times, the number of chromosomes is the same for cattle and goats, each of which have 29 acrocentric autosomes, as compared to the sheep which has only 26 autosomes (three metacentric, 23 acrocentric). The domestic sheep karyotype appears to have resulted from three Robertsonian translocation events resulting in sheep (OAR) chromosome 1 being equivalent to goat (CHI) and cattle (BTA) chromosomes 1 and 3, OAR 2 being equivalent to CHI/BTA 2 and 8, and OAR 3 being equivalent to CHI/BTA 5

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and 11 (Fig. 1). Other features of gross chromosomal morphology, such as the architecture of the X chromosome and that of OAR 9/CHI 14, are similar for sheep and goats, but differ from cattle [7, 11, 14, 17, 22, 27]. The similarity between the goat and sheep karyotypes is further evidenced by reports of natural matings between rams and does producing hybrid offspring, with at least one instance of such a mating generating a female offspring that was shown to be fertile when mated to a ram [16, 24, 25].

For both sheep and goats much of the impetus for genetic map development has come from the linkage mapping of traits of interest. In the case of goats, the reason for developing a genetic map was to map the locus responsible for the Polled Intersex Syndrome [26], and relatively little genetic map development has occurred for goats since this locus was mapped. Initially, much of the work on the sheep genetic map was aimed at identifying loci responsible for fertility traits such as Inverdale and Booroola [12, 20]. More recently mapping efforts in sheep have also included searches for traits affecting meat, wool, and disease susceptibility and resistance [4, 5, 8, 15]. This focus on mapping specific traits has lead to genetics maps that have uneven distributions of markers on chromosomes. Not surprisingly, regions disproportionately rich in markers are found in areas of the maps that are near traits of interest, *e.g.*, chromosome 6 with Booroola and Spider Lamb Syndrome, chromosome 18 and callipyge/Carwell, and the X chromosome and Inverdale in sheep; and chromosome 1 with Polled Intersex Syndrome in goats [6, 12, 21, 29, 30]. More recently development of the sheep genetic map has focused on increasing the number of mapped markers that are associated with genes so as to increase the number of links to maps of other species such as humans and mice [18]. This has mainly been done by the development and mapping of microsatellites that are associated with genes, and by performing blast searches to identify genes that are associated with previously mapped anonymous microsatellites. A brief summary of the development of the sheep and goat linkage maps is given in Table I.

2. MATERIAL AND METHODS

Construction of SheepMap 4.2 and alignment of sheep and goat genetic maps

The methods used for all aspects of map construction of the sheep genetic map are described in [17]. The current version (4.2) best positions sheep genetic map [3] was aligned with the most recent goat linkage map [23].

Table I. Map and population statistics for sheep and goat maps.

Map	Size (cM)	Map Type	Herd/Flock# Number of Animals	Number of Markers	Reference
Goat 1996	2300	Male	INRA 575	219	[27]
Goat 1998	2737	Male	INRA 575	307*	[23]
SheepMap 1	2070	Both sexes	IMF 127	246	[7]
SheepMap 2	3063	Both sexes	IMF, MARC 127 + 295	519	[9]
SheepMap 3	~3600	Both sexes	IMF 127	1093	[17]
SheepMap 4.2	~3600	Both sexes	IMF 127	1251	[3]
Sheep X, Y	141.9	Both sexes	XMF 480	21	[11]

*15 markers were mapped by fluorescent *in situ* hybridisation.
#The INRA goat herd consists of 12 2-generation families, the IMF (international mapping flock) consists of 9 3-generation full-sibling families, the MARC (Meat Animal Research Centre) flock consists of 4 2-generation families, and the XMF (X mapping flock) consists of 14 3-generation half-sibling families.

3. RESULTS

Details of the current sheep genetic map can be found on the Australian Gene Mapping Web Site [3] and in Table II. There are 1251 markers representing 1232 loci on the current sheep genetic map, and the comprehensive sex averaged genetic map spans approximately 3630 cM. This corresponds to virtually complete coverage of the sheep genome. Each chromosome is represented by a single linkage group with the largest gap between adjacent loci being 19.8 cM (*BMC1222–\BM8115* on chr 13 and *CGBP–\URB031* on chr 23). There are 74 regions on this map where the closest distance between adjacent markers is between 10 and 20 cM.

In contrast, the goat map is quite primitive. The only genetic map available is a male map that spans 2737 cM and comprises 307 markers. Only one of the chromosomes appears to have complete coverage (chromosome 27), with 16 of the chromosomes being comprised of 2 or more linkage groups, or a linkage group and one or more unlinked markers.

Table II. Chromosomal statistics and comparisons for the sheep best positions linkage map v 4.2.

OAR	Length of chromosome Sex Av cM	Female cM	Male cM	Number of sheep loci	Number of loci with highly polymorphic markers[#]	Number of loci on both sheep linkage and human maps	Number of loci mapped by linkage analysis in both sheep and goats
1	347.4	326.6	371.7	122	60	25	23[*]
2	308.4	289.5	328.5	106	59	24	21
3	313.4	305.1	319.6	103	45	27	18
4	151.9	136.2	159.9	44	18	12	9
5	156.9	154.0	168.8	46	12	12	8
6	156.7	132.2	178.9	64	26	25	7
7	145.9	141.0	250.9	55	25	16	8
8	132.8	133.7	131.5	41	22	8	7
9	126.9	118.5	134.7	43	32	8	12
10	105.1	102.2	108.7	34	19	2	6
11	112.4	106.6	120.4	41	16	19	7
12	113.1	98.2	127.7	33	16	7	5
13	128.3	128.0	128.7	35	18	6	4
14	119.9	98.4	141.3	40	26	8	8
15	124.4	100.9	145.9	47	25	19	7
16	86.2	78.9	92.4	35	20	6	10
17	130.7	118.5	143.6	41	20	9	9
18	131.5	115.3	151.7	46	22	8	7
19	73.3	67.8	85.3	27	15	6	6
20	89.6	80.4	103.0	32	13	10	7
21	74.2	59.2	87.1	26	15	6	4
22	82.9	60.6	98.7	22	14	3	6
23	95.5	84.1	106.6	21	10	7	5
24	89.4	89.2	90.1	31	11	12	3
25	69.9	56.2	78.8	20	11	4	2
26	71.1	57.3	85.9	20	12	2	9
Total autosomal	3537.8	3238.6	3940.4	1175	562	291	218
X	90.8	132.4	58.6	57	20	10	

[*]Two markers from the *PISRT1* region (LSCV86 and LSCV210) have been linkage mapped in both sheep and goats however these markers are not on the 1998 goat map [23].
[#]PIC of at least 0.7 or at least 8 alleles.

Table III. Mapping discrepancies between the genetic maps of sheep and goats.

Marker	OAR	Predicted CHI	Actual CHI	Comment
OarCP9	9	14	16*	Goat product sequence > 90% similar to sheep sequence
OarHH22	21	29	16	Cattle position equivalent to sheep
BM723	23	24	3*	Cattle position equivalent to goat
MAF48	X	X	19	

*Also mapped physically.

The sheep and goat genetic maps have 218 loci in common (Fig. 1, Tab. II). Overall there is good agreement between the maps in terms of loci mapping to equivalent chromosomes in the two species. There are only four markers that map to non-equivalent chromosomes (Tab. III). However, as can be seen in Figure 1, there are lots of inversions in locus order between sheep and goat chromosomes.

Both the sheep and goat maps have been mapped using a mixture of sheep, cattle and goat markers. There are 50 markers of goat origin on the sheep genetic map, 531 sheep markers and 700 cattle markers. The goat genetic map comprises 41 goat markers, 49 sheep markers and 217 cattle markers.

There are 497 links between the current sheep genetic map and the MARC 2003 cattle genetic map [19], and 186 links between the goat and cattle genetic maps. The alignment between the sheep and cattle chromosomes on the genetic maps is much better than that for the sheep and goat genetic maps with a much lower proportion of rearrangements in locus order (data not shown, see sheep-cattle comparisons on [3]).

Homologous human loci can be identified for 291 of the loci on the current sheep genetic map (Tab. I), and for 24 of the loci on the goat genetic map. This allows links to be made between the human sequence map and the sheep and goat genetic maps, which enable predictions of the positions of non mapped loci in sheep and goats.

4. DISCUSSION

The large proportion of shared markers on the sheep, goat and cattle genetic maps makes it relatively easy to align the maps. In contrast to the good agreement in locus order between the sheep and cattle maps there are many rearrangements in order between these maps and the goat map. It is likely that many of the discrepancies in order between the goat map and the other maps

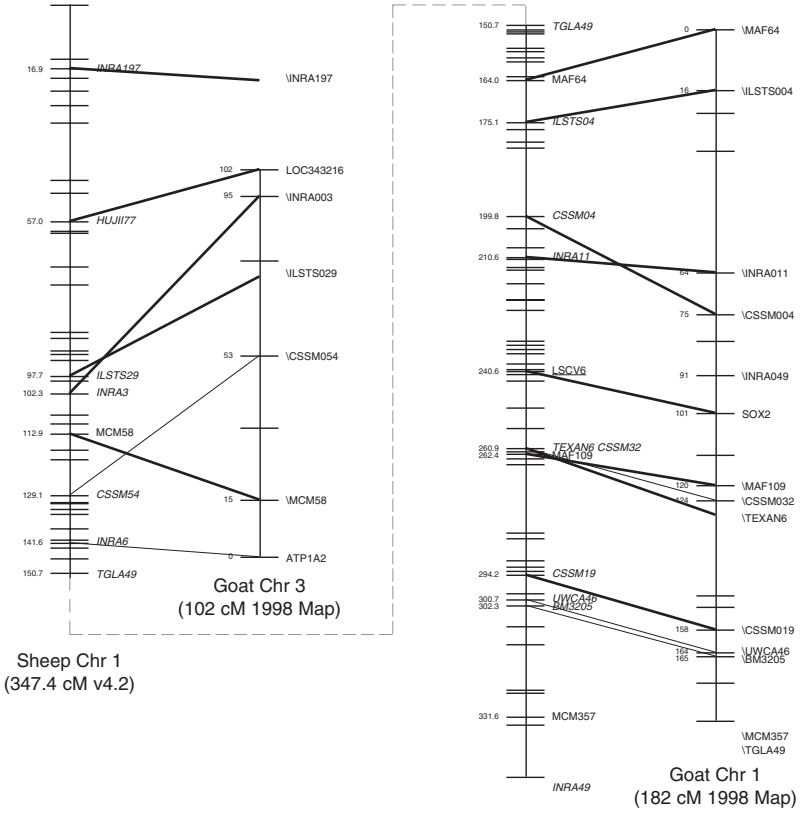

Figure 1. This figure shows the alignment of chromosome 1 from sheep and goat, as an example for the complete alignment of the current sheep linkage map (v 4.2) with the 1998 goat linkage map [23], which can be consulted at www.edpsciences.org/gse. Locus codes, marker names and position details are given only for markers that have been mapped by linkage analysis in both sheep and goats. Marker names are indicated beside sheep chromosomes and locus codes are given beside goat chromosomes. Horizontal lines on each chromosome are used to indicate the positions of all markers that have been mapped in sheep and goat. Cattle markers are indicated by italics, goat markers are underlined and sheep markers are indicated in normal text. ESTs are prefaced by a ~, anonymous loci are prefaced by a \ [1]. Loci that have been linkage mapped in sheep, but not on the IMF, are indicated either at the bottom of the appropriate chromosome or at their estimated position on the chromosome. The INRA197, MCM357 and TGLA49 markers did not link to other markers on the goat map. The \INRA197 locus has been physically mapped in goats and its physical position (3q36) indicates that it maps to the bottom of chromosome 3 (hence its placement in this figure). Thick lines between chromosomes are used to indicate loci that are on the sheep framework map, thin lines indicate loci where the position on the sheep map is supported by odd scores of less than 1000:1.

are artefacts. The goat genetic map is less robust, than the sheep and cattle maps, as a consequence of being constructed from a smaller number of markers. In addition, the amount of error checking that has taken place for the goat map is likely to be considerably less than has been done for either the sheep or cattle maps. However, it is possible that some of the discrepancies in chromosomal locations or locus order may be genuine. Given that the sequence of the goat product obtained using the OarCP9 primers was more than 90% similar to that of sheep [27], it is possible that homologous products are amplified in sheep and goats using these primers, and that the discrepancy in the chromosomal locations of these loci in sheep and goats is real. Likewise, the relative inversion of the order of the segment comprising *IL2RA–\ILSTS59* on chromosome 13 may be real. This order is based on cytogenetic mapping in the goat as there is insufficient linkage information to determine the order on the goat chromosome.

The lack of development of the goat map is not surprising given that the goat map was developed specifically for a genome screen to map a single Mendelian trait, and that the region containing this locus was identified without the need for a full genome scan [26]. The only region mapped in depth on the goat genetic map is the region on chromosome 1 flanking the *PISRT1* locus [21, 28]. In contrast, the sheep genetic map has benefited from being needed for genome screens for a variety of traits.

There has been a relatively greater effort in the goat to cytogenetically map loci [23], with almost 500 loci mapped cytogenetically [13]. This contrasts with the sheep where only about 350 loci have been cytogenetically mapped [2]. One hundred and thirty-two of the microsatellites (43%) on the goat genetic map have also been cytogenetically mapped, and 143 loci (12%) on the sheep map have also been cytogenetically mapped. In both sheep and goats the majority of the cytogenetically mapped loci are type I rather than type II (anonymous) loci, and thus the cytogenetically mapped loci have a greater proportion of links to homologues on the human sequence map than do the loci on the genetic maps.

To date, five mutations for single gene traits have been successfully mapped in sheep and goats following the use of the genetic maps of these species. These are the Spider Lamb [6], Booroola [30], Callipyge [10] and Inverdale [12] traits in sheep, and the Polled Intersex trait in goats [21]. Many QTL regions have been identified for a vast range of traits from genome screens in sheep. Whilst some of these QTL studies have advanced to the fine mapping stage, none of the sheep QTL studies has yet resulted in the identification of a causative mutation. Further genetic map development is needed to improve the efficiency

of genome screens in sheep and goats especially in terms of a more uniform coverage of map regions with highly polymorphic markers. It will also be vital to increase the number of links between the sheep and goat genetic maps and the sequence maps of other species, so as to be better able to use comparative information to assist with genome screens for traits of interest in sheep and goats.

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